ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

KidneyNews

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Researchers See Potential Marker for Renal Transplant Tolerance

By Eric Seaborg

Researchers described a biomarker signature associated with renal transplant tolerance in the absence of immunosuppressive drugs in a recent paper, with the novel news that the signature is related to B-cell genes and expression. The findings provide a tentative first step toward the goal of identifying patients whose immunosuppressive dosage could be tapered down through a better means than trial and error.

The vast majority of transplant patients who stop immunosuppression lose their kidneys to rejection, so it took five years and a countrywide search to identify a cohort to study. The study defined tolerance as going off immunosuppression and maintaining function at least one year later. The 25 patients involved made it the largest such study yet. Twenty of the patients had ceased taking their drugs because of medical noncompliance and five patients stopped under medical supervision because of complications. The researchers compared their gene expression profiles and peripheral blood lymphocyte subsets with those of a group of patients with stable graft function while on immunosuppression and a group of healthy controls with no transplants.

"We found that tolerant patients exhibited increased numbers of total and naïve B cells and had enhanced expression of B cell differentiation and activation genes compared with subjects receiving immunosuppression," the article notes. "Most notably, the tolerant cohort differentially expressed three B cell genes that were highly predictive of tolerance in a new test set of patients."

"Identification of a B cell signature associated with renal transplantation in humans" was published in the June issue of the *Journal of Clinical Investigation*. The research was a project of the Immune Tolerance Network, a consortium funded by the National Institute of Allergy and Infectious Diseases and the National Institute of Diabetes and Digestive and Kidney Diseases (1).

These three B-cell genes provided a

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Local Poverty Affects Kidney Disease Care

Poor Communities Use Fewer Arteriovenous Fistulas for Hemodialysis

By Tracy Hampton

The wealth or poverty of patients' communities often impacts the care they receive. Researchers recently discovered that this appears to be true for certain aspects of care for end stage renal disease (ESRD)—in particular, the use of an incident arteriovenous fistula (AVF) for hemodialysis vascular access.

Surprisingly, though, the intensity of poverty in the county where a treatment is located was not associated with subsequent AVF use among prevalent patients. The findings suggest that poverty's effects on AVF use may be mitigated by the Medicare ESRD program, through which Medicare reimburses the costs of ESRD care for all individuals eligible for Social Security benefits regardless of other patient characteristics.

Variability of care

There is substantial geographic variability in the use of AVF for patients with ESRD, despite the knowledge that AVF use for hemodialysis access is safe and is associated with improved survival. The National Kidney Foundation's Clinical Practice Guidelines for Vascular Access recommends early placement and use of an AVF among patients expected to re-

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Inside

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Reference: 1. Renvela [package insert]. Cambridge, MA: Genzyme Corp; 2009.

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Renal Transplant Tolerance

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signature of tolerance, although the researchers were quick to note that they have identified only an association with no cause-and-effect implied. A great deal of further research is needed before considering clinical applications of the findings, but observers have said it is an important first step.

The B cell connection surprised the researchers, who expected tolerance to be related to regulatory T cells, according to one of the study's authors, Kenneth A. Newell, MD, PhD, professor of surgery and director of the living donor kidney program at Emory University in Atlanta. "We were surprised that our data showed that B cell genes may play an important role in maintaining and possibly inducing tolerance to transplanted organs."

Other observers noted that while most attention has been devoted to T cells in recent years, the pendulum may be swinging toward B cells. "We have been very T cell centric," said Bruce Kaplan, MD, professor of medicine, pharmacology, and surgery and medical director of transplants at the University of Arizona in Tucson. "We've been looking at these T regulatory cells forever. We have done everything we can with inducing T regulatory cells, studying them, defining them, and it's satisfying to see that maybe the answer is somewhere else. It is still hard to understand what the mechanism would be for a B cell to have this effect, but it's nice to know that there is a whole new world to look at."

Kaplan was a co-author of a study in the same issue of *JCI* that examined gene expression profiles from biopsies of 105 kidneys that failed (2). The authors proposed a molecular risk score based on some 600 genes to predict incipient graft failure.

"There are mouse model data that say that B cells contribute to tolerance," said Peter Heeger, MD, professor of medicine and director of transplant research at the Mount Sinai School of Medicine in New York City.

Of course, the study cannot distinguish whether the B cells were a cause of the tolerance, whether the tolerance was a cause of the B cells, or neither.

"It's important to point out the [study] doesn't tell you what the people looked like when they first got their transplants," Newell told *Kidney News*. "Maybe they just always had more of these cells. Maybe they were just born different. Maybe shortly after the transplant something happened, they got more, and that made them tolerant. The other possibility is something happened after that transplant that made them tolerant, they stopped all their drugs, and that these B cells cropped up later, because they were tolerant." The results also say nothing about how many people who rejected their grafts have the signature, because no such people were included in the study.

In fact, the only definite conclusion that can be drawn is the most direct one. "All it has shown is that the marker was present in those who had immunosuppression already withdrawn," said Titte Srinivas, MD, of the department of nephrology and hypertension at the Cleveland Clinic.

The association is solid, however. The researchers cross-checked their samples with another research team that published a companion article in the same issue of *JCI* (3). That study, performed under the auspices of the Immune Tolerance Network and the Indices of Tolerance European Union consortium, looked at an additional 11 similarly tolerant transplant recipients. The authors identified an immunological profile of the tolerant state that included an expansion of peripheral B and NK lymphocytes, fewer activated CD4+ T cells, a lack of donor-specific antibodies, donor-specific hyporesponsiveness of CD4+ cells, among other components.

The two groups shared samples to perform cross-validation studies that confirmed the association of the tolerant state with the B-cell related genes. "We were able to narrow this signature down to three genes that predicted tolerance with 100 percent accuracy in our test set of patients. Because we found that this signature of three genes was highly predictive for tolerance, a simple [polymerase chain reaction] assay may prove to be an easy test for screening kidney transplant patients that may benefit from weaning immunosuppression," the Newell article notes.

Newell's group is already planning follow-up studies. The researchers plan

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Renal Transplant Tolerance

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to enroll 250 patients who are doing well on immunosuppression to see how prevalent this signature is. In the recently reported study, in addition to being present in the tolerant patients, the signature was present in about 10 percent of the patients who were doing well on their immunosuppression drugs. "So we're going to try to confirm that in a larger study," Newell said. "If it was 10 percent, you could envision other studies down the road to begin to explore whether the signature was actually useful."

Newell noted that a percentage around that level would be a hopeful sign for its clinical application. If a high number of immunosuppressed patients carried the signature, the information would not be useful because it is already known that most patients cannot go off drugs. If the percentage were much lower, it would identify very few patients who might benefit.

Such studies "may help to guide drug withdrawal in selected stable patients, limiting toxicity caused by long-term treatment with immunosuppressive agents. Only appropriately designed, prospective, randomized trials will determine whether the promise of a molecular crystal ball that predicts transplant outcome will evolve into reality," Heeger noted in a commentary that accompanied the three *JCI* articles (4).

Both Kaplan and Srinivas voiced worries that the study could be oversold in the lay press or misinterpreted by patients who see it on the Internet, leading patients to ask if they could be tested for this marker to lessen their amount of immunosuppression, when any clinical applications of the findings are years away.

Srinivas thought the study was also open to misinterpretation because of the use of words like "predictive." "Typically these studies get reviewed by other basic scientists, and they tend to use the word prediction rather loosely sometimes," he said. "When you start using words like prediction, that becomes a problem because you are implying causation, in other words, that this B cell signature is somehow positively linked to the process of tolerance," even though the authors note in other parts of the paper that they have found only an association.

Srinivas also noted that this was a cross-sectional study in which the recipients were very well-matched with their donors, so the results can only be considered to be directly applicable to the type of patient included in the study, and may not generalize to a larger population. The study itself notes that "many clinical factors associated with tolerance in this study are also known to identify low-risk kidney transplant recipient populations. Clinically, our [tolerant] cohort received well-matched kidneys from living donors," rather than the cadaveric kidneys that most recipients receive, and which are well-known to have a lower long-term success rate.

"This kind of thing is a very good first step, but I'd wait for long-term studies before I'd start saying this is a marker that allows us to predict other patients that can go off immunosuppression," Srinivas said, while at the same time noting that "this is on the cutting edge of translation research in transplantation."

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Local Poverty

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quire hemodialysis.

The reasons why AVF use differs among patient groups and geographic regions are unclear, but investigators suspect that poverty may play a role. Indeed research indicates that treatment centers with low rates of AVF use among incidence patients tend to cluster geographically. These center-to-center and regional variations cannot be accounted for by individual patient characteristics (McClellan WM, et al. *J Am Soc Nephrol* 2009; 20:1078–1085).

William M. McClellan, MD, MPH, of Emory University's division of nephrology and Rollins School of Public Health, in Atlanta, and his colleagues designed a study to examine the degree to which incident and prevalent AVF use are associated with the poverty in the county where a treatment center is located. They hypothesized that higher community poverty levels would reduce the proportions of patients using both incident and prevalent AVF.

AVF use and regional poverty

To conduct the analysis, the research team performed a cross-sectional study of 28,135 patients who were treated by 1127 hemodialysis centers in five ESRD networks within 16 states between June 1, 2005, and May 31, 2006. The 2000

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Local Poverty

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U.S. Census was used to categorize county-level poverty, and incident AVF use was ascertained from the Medicare CMS 2728 form. The change in prevalent AVF use over 30 months was calculated from monthly facility reports collected between 2003 and 2005.

An increased concentration of poverty in a treatment center's county was associated with both lower incident and baseline prevalent AVF rates, the investigators found. In contrast, prevalent AVF rates increased substantially over the 30 months of observation, from 30.9 percent to 38.6 percent. There was no significant association between county poverty concentration and the rate of change in prevalent AVF use. While it was no surprise that centers in poor communities recorded less effective AVF care for incident patients, McClellan and his co-investigators did not expect that the center-specific rate of increase in prevalent AVF use over a 30-month period would be independent of poverty.

"Our research suggests that the community where a treatment center resides may contribute to variations in pre-dialysis care," McClellan said. "This observation provides support for the development of quality improvement interventions targeted at these poorly performing communities and raises questions as to why poverty plays a role in community-to-community variations in care which are not seen following the start of dialysis."

That local poverty was not tied to the rate of increase in prevalent AVF use suggests that poverty's effects on AVF placement are malleable. Programs conducted to promote improved AVF care may help address the low rates of incident AVF use in poor areas. Treatment center-specific improvement in prevalent AVF use was measured during a national systematic effort to improve AVF rates, the authors said. So participation in the Medicare ESRD program may have mitigated the effect of poverty on disparities in ESRD treatment. This mitigation may reflect participation of treatment centers in mandated quality improvement activities.

Why local poverty might affect AVF use

Other experts in the field offered mixed reviews of the study's findings.

"I'm not sure that the article demonstrates the relationship quite as clearly as claimed," said Richard Hirth, PhD, professor of health management and policy and associate director of the Kidney Epidemiology and Cost Center at the University of Michigan School of Public Health, in Ann Arbor. "The authors did not control for any patient characteristics, even though they had some patient level data."

Hirth noted that there clearly is an association of incident AVF use with poverty, although a causal relationship cannot be drawn from this study. "That said, to the extent that the relationship is causal, I would expect that fewer and/or lower quality medical resources both before dialysis and in the dialysis center would contribute," he said. Clinics in areas with more privately insured patients are likely to have greater resources and that may benefit all patients, he explained.

Allen Nissenson, MD, chief medical officer for DaVita, Inc., one of the largest independent dialysis services providers in the country, noted that underserved communities are more likely to have fewer specialists, including nephrologists, less preventive care and screening, and a higher severity of chronic diseases with attendant higher mortality and morbidity. "This creates a significant disease burden for patients and a cost burden for society," he said.

McClellan and his team suspect that the knowledge of local primary care physicians might also vary with regional poverty, leading to delays in referrals for AVF placement. In addition, poorer communities might negatively influence opinions, attitudes, and beliefs among individuals with advanced kidney disease about the utility of early AVF surgery. Aggressive screening and educational programs to identify patients with CKD and get them to see a nephrologist early might increase incident AVF use in poor communities, said Nissenson.

ASN News

Renal Week 2010 to Feature World-Renowned Speakers

Renal Week 2010 will be held November 16 to 21 in Denver. Our program and postgraduate education committees have selected a number of exciting lectures, and ASN will honor world-renowned leaders through our awards presentations and endowed lectureships. This year's state-of-the-art lectures, award recipients, and endowed lectureships are outlined here.

State-of-the-Art Lectures

Mapping Genes for Complex Traits Using the Canine System
Elaine Ostrander, PhD
Chief and Senior Investigator, Cancer Genetics Branch, National Human Genome Research Institute, National Institutes of Health

From Data to Knowledge to Wisdom: Improving Practice and Policy in the 21st Century
Harlan M. Krumholz, MD, SM
Harold H. Hines, Jr., Professor of Medicine and Epidemiology and Public Health, Yale University School of Medicine

Blocking IL-1β in Auto-inflammatory Diseases
Charles A. Dinarello, MD
Professor of Medicine, Division of Infectious Diseases, University of Colorado School of Medicine

New Insights, Surprises, and Lessons about the Pathogenesis for Cystic Fibrosis Pigs
Michael J. Welsh, MD
Professor of Medicine, Molecular Physiology and Biophysics, and Neurosurgery, Roy J. Carver Biomedical Chair in Internal Medicine, Investigator, Howard Hughes Medical Institute, University of Iowa Carver College of Medicine

ASN Awards and Addresses

Belding H. Scribner Award
Hans-Henrik Parving, MD, DMSc
Chief Physician Professor, Department of Medical Endocrinology, National Hospital, University of Copenhagen

Homer W. Smith Award and Address
Wilhelm Kriz, Dr. Med
Professor Emeritus of Anatomy, Department of Anatomy and Cell Biology, University of Heidelberg
The Impact of Morphology on Renal Research

John P. Peters Award
Roland C. Blantz, MD, FASN
Head, Division of Nephrology-Hypertension, Professor of Medicine, University of California, San Diego, School of Medicine

Robert G. Narins Award
Barry M. Brenner, MD
Samuel A. Levine Distinguished Professor of Medicine, Harvard Medical School; Director Emeritus, Renal Division, Brigham and Women's Hospital

Young Investigator Award and Address
Nicholas Katsanis, PhD
Director, Center for Human Disease Modeling, Professor, Departments of Cell Biology and Pediatrics, Jean and George W. Brumley Distinguished Professor, Duke University School of Medicine
The Genetic Architecture of Ciliary Disorders

Endowed Lectureships

Barry M. Brenner Endowed Lectureship
Rama Natarajan, PhD, FASN
Professor, Diabetes, Endocrinology and Metabolism, Professor, Diabetes, Gene Regulation and Drug Discovery, City of Hope
TGF-beta and MicroRNAs in Diabetic Nephropathy

Christopher R. Blagg Endowed Lectureship in Renal Disease and Public Policy
Patricia A. Gabow, MD
Chief Executive Officer, Denver Health and Hospital Authority
Healthcare Delivery and Reform: Relegitimizing Common Sense

Jack W. Coburn Endowed Lectureship
Keith A. Hruska, MD
Professor of Pediatrics, Medicine, and Cell Biology, Director, Division of Pediatric Nephrology, Washington University in St. Louis, School of Medicine
CKD-MBD: The Bone-Gut-Kidney Connection

Robert W. Schrier Endowed Lectureship
Richard A. Zager, MD
Professor, Division of Gerontology and Geriatric Medicine, University of Washington
Biologic Memory in Acute Renal Failure

ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

Flat Funding for the NIDDK an Impediment to Kidney Research

A Three-Part Series Looking at NIDDK Funding

By Daniel Kochis

Part I: A Historic Retrospective

The National Institute of Arthritis and Metabolic Diseases, predecessor of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), was founded in 1950 under the already established National Institutes of Health (NIH). The end of World War II and the subsequent economic boom shifted dollars and scientific brainpower into medical research as never before. The decade after World War II saw the establishment of no fewer than six divisions of the NIH, including the future NIDDK and the National Heart, Lung, and Blood Institute. The research undertaken by the NIH and its new institutes contributed greatly to public health, raising Americans' life expectancy from 68 years in 1950 to its current level of 78 years.

NIDDK sponsored research has dramatically improved the lives of people suffering from kidney disease.

In the years since its establishment, the NIDDK, which is celebrating its 60th anniversary this year, has advanced our understanding of and ability to treat major public health concerns, including kidney disease. In 1948, kidney disease was the fourth leading cause of death in the United States; by 1949, it had dropped out of the top 10, falling to 20th by 1960. Although the drop can be attributed to several factors, advances in kidney disease treatment—in large part funded by the NIDDK—played a leading role in this progress. However, death rates from kidney disease began to steadily lurch forward in the next two decades, culminating in kidney disease reaching the dubious distinction of being the ninth leading cause of death in the United States in 1997 (1). Today, kidney disease remains the ninth leading cause of death for Americans, with roughly one in nine citizens suffering from chronic kidney disease and a higher level of mortality in certain minority populations. Furthermore, the increase in obesity, hypertension, and diabetes has greatly contributed to the rise in kidney disease in the United States over the past 20 years.

The history of kidney disease mortality is crucial for an understanding of the need for NIDDK funding, for two reasons. First, it reveals the tremendous contribution NIDDK-funded research has had in slowing the progression of kidney disease and the mortality of chronic kidney disease (Figure 1). Second, it underscores the importance of NIH funding for today's research efforts. Sharon Anderson, MD, FASN, president of the American Society of Nephrology, explained: "For kidney disease treatment, we would not have advanced as far as we have without the catalyzing effect of the NIDDK. NIDDK-sponsored research has dramatically improved the lives of people suffering from kidney disease."

As the disease continues to claim a significant number of lives every year, both human and financial costs continue to expand. Despite the number of lives it claims, however, extramural funding for kidney disease through the NIDDK lags behind the external research dollars spent on other diseases (Figure 2).

The NIH spent $523 million on kidney disease research in 2008 (2). But with a population expanding and aging simultaneously, is this funding enough? The bull market of the 1990s led to a doubling down on medical research with funding for the NIH. In 1998, President Clinton and Congress agreed to double the budget of the NIH over the next five years. The impact of this investment was significant, yet despite the positive effect of the increased budget on renal research (the subject of the next installment of this series), the increase was temporary. In 2006, the NIH's budget did not keep pace with inflation for the first time in 30 years (3). Furthermore, a gulf has developed between NIDDK funding and the funding for some of the larger NIH institutes over the past 20 years (Figure 3).

When asked about the NIDDK's recent funding, John Sedor, MD, said: "Although the NIDDK budget has more than doubled in the past 20 years, the increases in appropriated dollars to NIDDK when compared to funding increases for other institutes, while appreciated by the kidney community, have been more modest." Although the number of people suffering from kidney-related diseases has increased since 1990, the NIDDK's percentage of the NIH budget has decreased from 8.5 percent in 1990 to 7.8 percent in 2010 (4). The ASN continues to advocate for increased funding for the NIDDK and kidney disease research. The current state of NIDDK funding will be the focus of our next discussion, with a particular emphasis on NIDDK-funded research grants.

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Next month's installment of this series will address "NIDDK Kidney Research in Real Time, the Current State of Funding, and its Impact on Science."

Interested in additional information on trends in NIDDK funding? Check out the ASN Public Policy Website at http://asn-online.org/policy_and_public_affairs/

Figure 1. Key milestones in NIDDK-supported research efforts

1953: U.S. Public Health Service–funded researchers purify what is later identified as erythropoietin

1988: The United States Renal Data System is created, allowing for better clinical management of kidney disease while assisting kidney researchers through improved data collection and analysis

1994: The Modification of Diet in Renal Disease Study presents findings that lead to an equation that estimates kidney function

1995: The African American Study of Kidney Disease and Hypertension trial begins; the longest and largest study of chronic kidney disease in African Americans, it helps researchers understand the best treatment to slow kidney disease in African Americans with high blood pressure

2002: The Hemodialysis Study finds that a standard dose of dialysis works as well as higher doses in most situations

2008: The Veterans Affairs/National Institutes of Health Acute Renal Failure Trial Network Study findings show that standard dose dialysis works as well as higher doses in patients with acute kidney failure

Figure 2. 2009 budget authority by NIDDK program

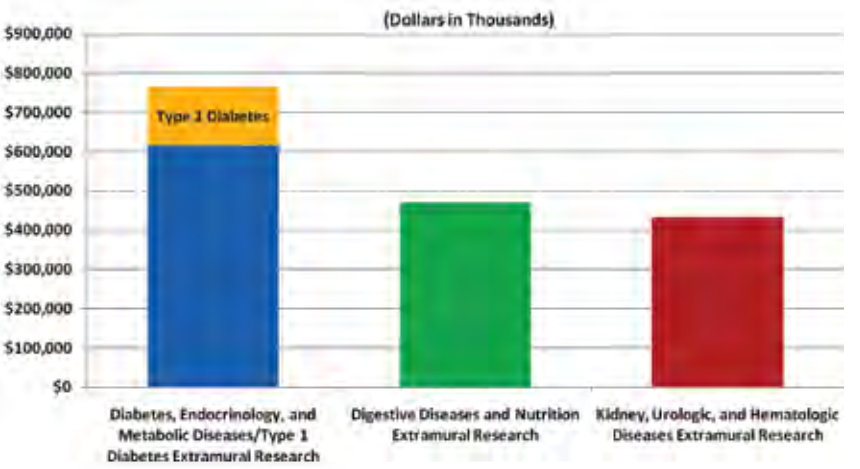
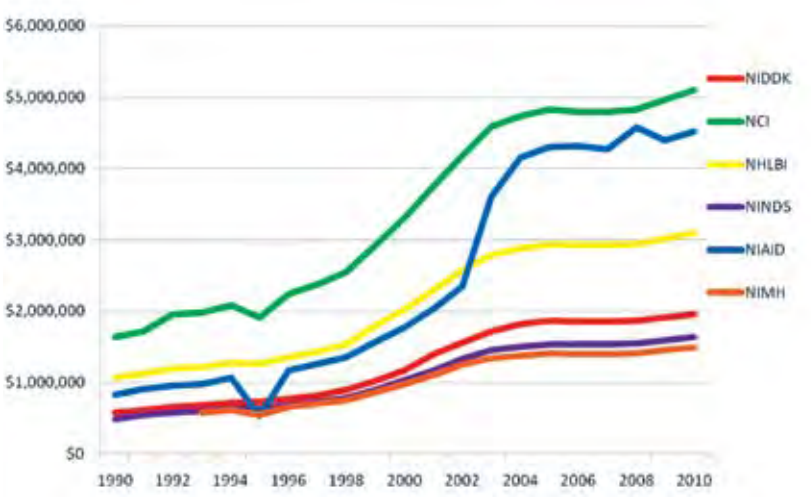


Figure 3. Funding since 1990 for selected NIH institutes



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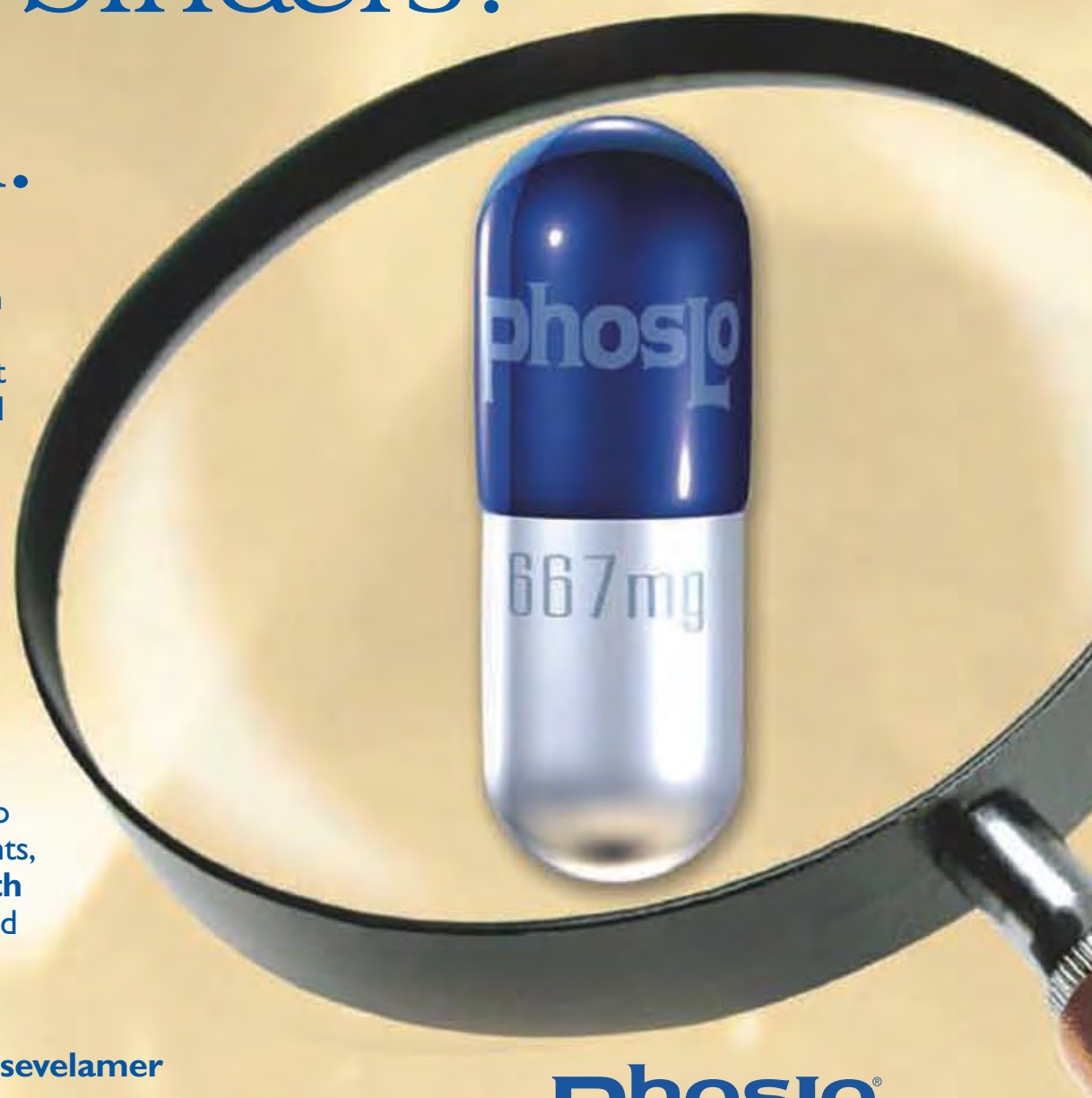

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CONTRAINDICATIONS: Patients with hypercalcemia. INDICATIONS AND USAGE: For the control of hyperphosphatemia in end-stage renal failure. WARNINGS: Patients with end-stage renal failure may develop hypercalcemia when given calcium with meals. No other calcium supplements should be given concurrently with PhosLo. Progressive hypercalcemia due to overdose of PhosLo may be severe as to require emergency measures. Chronic hypercalcemia may lead to vascular calcification, and other soft-tissue calcification. The serum calcium level should be monitored twice weekly during the early dose adjustment period. The serum calcium times phosphate (Ca x P) product should not be allowed to exceed 66. Radiographic evaluation of suspect anatomical region may be helpful in early detection of soft-tissue calcification. PRECAUTIONS: Excessive dosage induces hypercalcemia; therefore, early in the treatment during dosage adjustment serum calcium should be determined twice weekly. Should hypercalcemia develop, the dosage should be reduced or the treatment discontinued immediately depending on the severity of hypercalcemia. Do not give to patients on digitalis, because hypercalcemia may precipitate cardiac arrhythmias. Always start PhosLo at low dose and do not increase without careful monitoring of serum calcium. An estimate of daily calcium intake should be made initially and the intake adjusted as needed. Serum phosphorus should also be determined periodically. Information for the Patient: Inform the patient about: 1) compliance with dosage, 2) adherence to diet instructions and avoidance of nonprescription antacids, and 3) symptoms of hypercalcemia. Drug Interactions: PhosLo may decrease the bioavailability of tetracyclines. Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term animal studies have not been performed. Pregnancy: Teratogenic Effects: Category C. Animal reproduction studies have not been conducted. It is not known whether PhosLo can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Give to a pregnant woman only if clearly needed. Pediatric Use: Safety and effectiveness in pediatric patients have not been established. Geriatric Use: Of the total number of subjects in clinical studies of PhosLo (n = 91), 25 percent were 65 and over, while 7 percent were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. ADVERSE REACTIONS: In clinical studies, patients have occasionally experienced nausea during PhosLo therapy. Hypercalcemia may occur during treatment with PhosLo. Mild hypercalcemia (Ca>10.5 mg/dl) may be asymptomatic or manifest itself as constipation, anorexia, nausea and vomiting. More severe hypercalcemia (Ca>12 mg/dl) is associated with confusion, delirium, stupor and coma. Mild hypercalcemia is easily controlled by reducing the PhosLo dose or temporarily discontinuing therapy. Severe hypercalcemia can be treated by acute hemodialysis and discontinuing PhosLo therapy. Decreasing dialysate calcium concentration could reduce the incidence and severity of PhosLo induced hypercalcemia. The long-term effect of PhosLo on the progression of vascular or soft-tissue calcification has not been determined. Isolated cases of pruritus have been reported which may represent allergic reactions. OVERDOSAGE: Administration of PhosLo in excess of appropriate daily dosage can cause severe hypercalcemia (see ADVERSE REACTIONS).

For more information on PhosLo®, please contact Fresenius Medical Care at **800-323-5188.**
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Journal View

Access to Transplantation Varies Among U.K. Renal Centers

British dialysis centers show significant variations in access to kidney transplantation, mainly in outcomes under the influence of center-specific practices, reports a study in the *British Medical Journal*.

Registry data were used to identify 16,202 patients starting renal replacement therapy at 65 U.K. renal centers from 2003 through 2005. Patients were followed up for transplantation or death, or through 2008. Between-center variations in kidney transplantation and related outcomes were assessed, with adjustment for case mix.

The patient-related factors affecting access to the waiting list or receipt of transportation were as in previous studies, with lower access for older patients, nonwhite patients, and those with diabetes. Even after adjustment for these factors, there were significant differences in access. In a risk-adjusted logistic regression model including renal center as a random effect, changes in the value of –2LogL were 89.9 for access to the transplant list, 247.4 for time taken to register patients on the waiting list, 15.1 for receipt of a kidney from a brain-dead donor, and 46.1 for receipt of a kidney from a living donor or donation after cardiac death.

In the United Kingdom, kidney transplants from brain-dead donors are nationally allocated, once patients are placed on the waiting list. Transplantation from a living donor or donation after cardiac death is influenced by renal center policies and practice.

The new analysis shows significant variations in access to transplantation at U.K. renal centers, after adjustment for case mix. The variations appear greater for outcomes affected by local center practices: time to waiting list placement and access to donors after cardiac death and living kidney donors. The authors call for further research "to determine whether the observed differences in centres' performance are due to variations in availability of resources or because certain centres have more organised and efficient pathways for patients." [Ravanan R, et al. Variation between centres in access to renal transplantation in UK: longitudinal cohort study. *BMJ* 2010; 341:c3451].

Pneumococcal Vaccine Linked to Shifts in Hemolytic Uremic Syndrome in Children

Data from Utah show an increase in pediatric hemolytic-uremic syndrome (HUS) caused by *Streptooccus pneumoniae* in the decade since introduction of routine pneumococcal vaccination, reports *The Pediatric Infectious Disease Journal*.

Using separate databases, the researchers identified 435 Utah children diagnosed with culture-confirmed invasive pneumococcal disease (IPD) between 1997 and 2008 and 460 children diagnosed with HUS between 1971 and 2008. Trends in the epidemiology of *S. pneumoniae*-induced HUS (SP-HUS) were analyzed, with special attention to the causative pneumococcal serotypes.

Overall, just 1.5 percent of pediatric HUS cases were caused by pneumococci and 1.6 percent of children with IPD had HUS. However, after introduction of the heptavalent pneumococcal conjugate vaccine (PCV-7) in 2000, there was a shift toward more cases of SP-HUS. The percentage of IPD cases that were HUS increased from 0.3 percent before 2000 to 5.6 percent afterward.

Pneumonia and empyema were more likely in children with SP-HUS, compared to other IPD cases. Forty-three percent of children with SP-HUS required dialysis and 33 percent had long-term renal sequelae. Pediatric SP-HUS was specifically associated with *S. pneumoniae* serotype 3, which is not covered by PCV-7.

An important cause of acute kidney injury in children, HUS is usually associated with bacteria causing diarrheal illness, rather than pneumococcal infection. The introduction of PCV-7 has reduced the rate of IPD, but also led to changes in the epidemiology of IPD.

The new results document an increasing incidence of SP-HUS in Utah children, largely attributable to a serotype not included in PCV-7. This is a serious complication requiring increased levels of acute care and associated with chronic renal morbidity. A new PCV-13 vaccine currently being considered for approval would cover serotype 3 [Bender JM, et al. Epidemiology of *Streptococcus pneumoniae*-induced hemolytic uremic syndrome in Utah children. *Pediatr Infect Dis J* 2010; 29:712–716].

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Falls in Dialysis Patients

By Beckie Michael, DO, FASN, on behalf of the ASN Practicing Nephrologists Advisory Group

More than one third of individuals aged 65 and older fall each year in the United States. The frequency of falls is even greater in dialysis patients, where it has been reported that 44 percent of elderly hemodialysis (HD) patients have more than one fall in a one-year period, at a rate of 1.6 falls per patient per year. A study by Desmet et al. (1) looked at falls occurring in 308 in-center HD patients and found an average incidence of 1.18 falls per patient year. One third of the falls in this study required health care intervention, and 3.9 percent resulted in a fracture. Independent risk factors for falling were older age, diabetes, number of prescribed medications, and antidepressant use. Even when an individual does not sustain an injury after a fall, that individual often develops a fear of falling, which results in a decrease in activity and further deconditioning.

One-year mortality in dialysis patients who have had a hip fracture is two to three times that of patients without end stage renal disease.

In older adults, falls are the leading cause of injury-related deaths. Falls in dialysis patients are also associated with significant morbidity and mortality. One-year mortality in dialysis patients who have had a hip fracture is two to three times that of patients without end stage renal disease. A study by Li et al. (2) found that after adjusting for comorbidities and dialysis vintage, more than one fall in an HD patient 65 or older was a significant predictor of mortality. There is also a significant financial impact of falls. In 2003, falls in the United States in individuals 65 and older cost $19.2 billion in direct medical costs—63 percent of the cost related to hospitalization, 21 percent to emergency room visits, and 16 percent to outpatient therapy.

One of the strongest predictors of fall risk is a history of having fallen. Risk factors for falling can be classified as intrinsic or extrinsic. Intrinsic factors (i.e., physical factors) include weakness, poor balance, vision deficits, medication side effects, and hypotension (Table 1). Dialysis patients are at particular risk of postural hypotension. Extrinsic factors (i.e., environmental factors) include uneven or wet flooring and poor lighting.

Once an individual is identified as having an increased risk of falls, interventions can include gait training and use of assistive devices, use of appropriate footwear, vision evaluation and correction, participation in an exercise program that improves balance and strength (such as Tai Chi), review and modification of medication, treatment of postural hypotension, and assistance with ambulation in the dialysis facility.

It has been recommended that HD patients who are at risk of falls be identified and participate in a fall prevention program. The Mid-Atlantic Renal Coalition has a 5-Diamond Safety Program module on Slips, Trips, and Falls. The staff and patient education modules include policies on fall risk assessment, prevention, and management and are available at http://www.esrd-net5.org/5DiamondSTFs.asp. The Centers for Disease Control and Prevention also has tools on its website (http://www.cdc.gov/HomeandRecreationalSafety/Falls), including posters, patient brochures, and fall prevention activities (Table 2). Implementation of these strategies should reduce fall incidence and improve outcomes in the dialysis patient population.

Beckie Michael, DO, FASN, is the co-medical director of the DSI Marlton Dialysis Center in Marlton, New Jersey. Michael is a member of the ASN Practicing Nephrologists Advisory Group.

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Further Readings

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Table 1. Fall risk assessment

If three or more of the following criteria are present, or if there is a history of falling, the patient is at increased risk of falling. Fall precautions should be instituted.

- Impaired vision or hearing
- Impaired mobility
- Orthostatic hypotension
- Age >70 years
- Medications affecting heart rate or blood pressure
- Altered mental status

Table 2. Fall precautions

- Assist patient with ambulation in unit before and after treatment
- Assist patient with bathroom visits
- Determine if physical therapy/gait and balance training and/or ophthalmology referral is indicated
- Encourage use of walking aid (e.g., cane or walker) if appropriate
- Evaluate patient's medications monthly and evaluate dry weight regularly
- Make sure patient's shoes fit appropriately and are tied
- Provide patient with the Centers for Disease Control and Prevention's "What You Can Do to Prevent Falls" brochure (available at http://www.cdc.gov/omeandRecreationalSafety/Falls/index-pr.html)

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Nephrology Workforce Shortage: Current Needs and Opportunities

By Suzanne Watnick and Paul Klotman

Now that federal health care legislation has passed, more Americans are forecast to seek primary care. The Association of American Medical Colleges anticipates a shortfall of 150,000 doctors over the next 15 years, implying the need for a 15 percent expansion of current numbers (1). Increased needs in the primary care setting are predicted to result in similar increases in subspecialty areas that provide consultative chronic care to patients, including nephrology. Expansion of new programs, such as subspecialist involvement in a comprehensive patient-centered medical home, could increase the demand for additional nephrologists further.

Nephrologist shortage

Are we prepared to meet the expanding need? According to past trends reported by the *Journal of the American Medical Association* in its annual "Graduate Medical Education" (GME) edition, the total number of nephrology fellows increased from 635 to 822 between 1998 and 2005. From 2005 to 2008, however, this number remained essentially unchanged, at 812 fellows in 2008 (2). Newer estimates are not optimistic. Preliminary data from the current National Residency Match program suggest that applications to nephrology fellowships have not increased over the last few years. The proportion of international medical graduates (IMGs) seeking nephrology fellowships, however, has increased from 41 to 53 percent of applicants over the period 2007 to 2008, and 49 percent of 2009 Fellowship Match applicants were IMGs, the second highest among subspecialties, after geriatric medicine (3). According to national GME census data from 2008, the average percentage of IMGs in a subspecialty is 27 percent, suggesting that fewer medical graduates in the United States are considering nephrology as a career.

What is the rationale for fewer graduates considering a field as gratifying as nephrology? Fewer students are choosing internal medicine as a specialty, limiting our traditional pipeline. In addition, student debt has risen over the last 20 years by 50 percent, after adjustment for inflation. Potential candidates often choose alternate, more lucrative subspecialties to pay the average monthly debt of $1700 (4). Additional survey data show that candidates are less interested in the rigors of nephrology as a general field (5).

One prediction of growth in the nephrology workforce was a 2 percent yearly expansion, based on 2005 data (6,7). This was predicated on an expansion in the number of nephrology fellows, which has since leveled out. In addition, the nephrology workforce is not getting any younger. January 2006 American Medical Association Masterfile data show that 30 percent of nephrologists were 55 years of age or older; in January 2008, this number increased to 34 percent. The aging of the current nephrology workforce combined with the failure to expand the number of new trainees will make it difficult for the nephrology community to meet the growing demand for services.

Patient population expanding

The most recent figures from the U.S. Renal Data System Annual Data Report reveal a new high of 527,283 prevalent ESRD patients, with an expected 50 percent increase in the next 10 years (8). The prevalence rates of ESRD have been increasing at 2 to 2.3 percent per year since 2003, a figure that is estimated to remain relatively constant. In addition to the expanding ESRD population, chronic kidney disease (CKD) patient numbers have increased. Data from National Health and Nutritional Examination Surveys estimate that the prevalence of CKD stage 3 through 5 increased from 10 percent to 13 percent of the U.S. population during the periods 1988–1994 and 1999–2002 (9). This did not include patients on dialysis. U.S. Renal Data System data showed similar findings (8).

In addition, there has been increased awareness of early stages of CKD through programs such as the National Institute of Health's National Kidney Disease Education Program with additional emphasis on CKD screening and nephrology referral. Current reforms will lead more people to seek medical care.

What can we do to change the tide?

"A key to growing the nephrology workforce is increasing the pipeline of trainees interested in the kidney," said Mark Rosenberg, section chief of nephrology at the Minneapolis VA Medical Center and former director of the renal fellowship program from 1996 to 2005. "We need to engage our students earlier in medical school with cutting-edge and innovative teaching. Nephrologists need to be role models for clinical and academic careers demonstrating excellence in delivering evidence-based and measurable care to our patients."

The ASN sponsors programs for medical students and residents through a number of forums, including national meetings, with specific pathways and speakers designed to generate heightened interest in the field. "At the ASN meeting, the program for residents was very well organized… but more than anything, I got excited about nephrology," said Tricia Jesperson, MD, a medical resident at the Oregon Health and Science University.

The National Kidney Foundation supports similar programs in which residents can interact with senior nephrology faculty and present their research in a supportive, engaging environment. After presenting his research at the National Kidney Foundation's annual meeting, Jacob Poulouse, MD, a medical resident at New York Hospital Medical Center, said: "Residents [become] more committed to nephrology as a result of these programs." The Renal Physicians Association offers free membership to fellows, with access to multiple resources to enter the workforce successfully.

These societies and others offer additional assistance, recognizing the need for strong support and encouragement of trainees. This can also be successful at the medical student level. Christina Chen, MD, a medical intern at Tufts University, said: "As a medical student, I was given the chance to present my project [at a national forum]… and that continued to increase my interest in nephrology." These opportunities to interact with mentors and other trainees are exciting for trainees and can generate enthusiasm to fill our future ranks.

We can lobby Congress to expand Medicare funding for the training and reimbursement of nephrologists. The Balanced Budget Act of 1997 capped the number of Medicare-funded GME training positions. Since then, expansion of nephrology positions has been funded through either redistribution of funds or nontraditional funding sources. Changes in health care are allowing for changes in distribution of slots for primary care trainees. Such changes should be considered for nephrology trainees, too.

We should continue to encourage and fund research that will decrease the burden of kidney disease in our patient population. Better diagnostic tools, techniques, and therapies may result in a decreased need for nephrologists. "The nephrology community should continue to work together as a unified force to lobby Congress on this issue," said Sharon Anderson, MD, president of the American Society of Nephrology and chief of medicine at the Portland VA Medical Center.

Although many a nephrologist loves the maintenance of a steady state, we must find ways to expand our ranks by offsetting retirees with new recruits. This need should re-energize us to do what we can to seek eager trainees, to communicate the excitement we hold for our field, and to provide mentorship to those who hold promise and interest in taking care of the next generation of patients with kidney disease.

Suzanne Watnick, MD, is associate professor of medicine and nephrology fellowship program director at Oregon Health and Science University and Paul Klotman, MD, is professor and chair, medicine, nephrology, as well as professor of gene and cell medicine at Mount Sinai Medical School in New York.

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IMPORTANT SAFETY INFORMATION: Venofer® (iron sucrose injection, USP) is indicated in the treatment of iron deficiency anemia in hemodialysis dependent-chronic kidney disease (HDD-CKD) patients receiving an erythropoietin, and peritoneal dialysis dependent-chronic kidney disease (PDD-CKD) patients receiving an erythropoietin. Venofer® is contraindicated in patients with evidence of iron overload, in patients with known hypersensitivity to Venofer® or any of its inactive components, and in patients with anemia not caused by iron deficiency. Hypersensitivity reactions have been reported with IV iron products. Hypotension has been reported frequently in HDD-CKD and PDD-CKD patients receiving IV iron, and may be related to rate of administration and total dose delivered.

In multi-dose efficacy studies in HDD-CKD patients, the most frequent adverse events (>5%), whether or not related to Venofer® administration, were hypotension, muscle cramps, nausea, headache, graft complications, vomiting, dizziness, hypertension, chest pain and diarrhea. In the study of PDD-CKD patients, the most frequent adverse events, whether or not related to Venofer®, reported by ≥5% of these patients were diarrhea, peritoneal infection, vomiting, hypertension, pharyngitis, peripheral edema and nausea.

*100 mg vials and ampules worldwide from 1992 to February 2009.

References: 1. Data on file. Fresenius Medical Care. Waltham, MA. **2.** Based on IMS Health, IMS National Sales Perspective™ (October 2009) 3rd quarter 2009 results-dollar volume ($) and units (100 mg equivalents).

Please see brief prescribing information on following pages.

Fresenius Medical Care
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Venofer®
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Brief Summary (See Package Insert For Full Prescribing Information)

Therapeutic Class: Hematinic

CLINICAL INDICATIONS AND USAGE

Venofer® (iron sucrose injection, USP) is indicated in the treatment of iron deficiency anemia in the following patients:

- hemodialysis dependent-chronic kidney disease (HDD-CKD) patients receiving an erythropoietin.
- peritoneal dialysis dependent-chronic kidney disease (PDD-CKD) patients receiving an erythropoietin.

CONTRAINDICATIONS

The use of Venofer® is contraindicated in patients with evidence of iron overload, in patients with known hypersensitivity to Venofer® or any of its inactive components, and in patients with anemia not caused by iron deficiency.

WARNINGS

Hypersensitivity reactions have been reported with injectable iron products. See **PRECAUTIONS** and **ADVERSE REACTIONS.**

PRECAUTIONS

General: Because body iron excretion is limited and excess tissue iron can be hazardous, caution should be exercised to withhold iron administration in the presence of evidence of tissue iron overload. Patients receiving Venofer® require periodic monitoring of hematologic and hematinic parameters (hemoglobin, hematocrit, serum ferritin and transferrin saturation). Iron therapy should be withheld in patients with evidence of iron overload. Transferrin saturation values increase rapidly after IV administration of iron sucrose; thus, serum iron values may be reliably obtained 48 hours after IV dosing. See **DOSAGE AND ADMINISTRATION** and **OVERDOSAGE.**

Hypersensitivity Reactions: Serious hypersensitivity reactions have been reported in patients receiving Venofer®. No life-threatening hypersensitivity reactions were observed in the clinical studies. Several cases of mild or moderate hypersensitivity reactions were observed in these studies. There are post-marketing spontaneous reports of life-threatening reactions in patients receiving Venofer®. See **ADVERSE REACTIONS.**

Hypotension: Hypotension has been reported frequently in hemodialysis dependent chronic kidney disease patients receiving intravenous iron. Hypotension also has been reported in peritoneal dialysis dependent-chronic kidney disease patients receiving intravenous iron. Hypotension following administration of Venofer® may be related to rate of administration and total dose administered. Caution should be taken to administer Venofer® according to recommended guidelines. See **DOSAGE AND ADMINISTRATION.**

Carcinogenesis, Mutagenesis, and Impairment of Fertility:

No long-term studies in animals have been performed to evaluate the carcinogenic potential of Venofer®.

Venofer® was not genotoxic in the Ames test, the mouse lymphoma cell (L5178Y/TK+/-) forward mutation test, the human lymphocyte chromosome aberration test, or the mouse micronucleus test.

Venofer® at IV doses up to 15 mg iron/kg/day (about 1.2 times the recommended maximum human dose on a body surface area basis) was found to have no effect on fertility and reproductive performance of male and female rats.

Pregnancy Category B: Teratology studies have been performed in rats at IV doses up to 13 mg iron/kg/day (about 0.5 times the recommended maximum human dose on a body surface area basis) and rabbits at IV doses up to 13 mg iron/kg/day (about 1 times the recommended maximum human dose on a body surface area basis) and have revealed no evidence of impaired fertility or harm to the fetus due to Venofer®. There are, however, no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: Venofer® is excreted in milk of rats. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Venofer® is administered to a nursing woman.

Pediatric Use: Safety and effectiveness of Venofer® in pediatric patients have not been established. In a country where Venofer® is available for use in children, at a single site, five premature infants (weight less than 1,250 g) developed necrotizing enterocolitis and two of the five expired during or following a period when they received Venofer®, several other medications and erythropoietin. Necrotizing enterocolitis may be a complication of prematurity in very low birth weight infants. No causal relationship to Venofer® or any other drugs could be established.

Geriatric Use: The five pivotal clinical trials did not include sufficient numbers of subjects aged 65 years and older to determine whether they respond differently from younger subjects. No overall differences in safety were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

ADVERSE REACTIONS

Adverse Events observed in all treated populations

The frequency of adverse events associated with the use of Venofer® has been documented in six randomized clinical trials involving 231 hemodialysis dependent and 75 peritoneal dialysis dependent-CKD patients; and in two post-marketing safety studies involving 1,051 hemodialysis dependent-CKD patients for a total of 1,496 patients. In addition, over 2,000 patients treated with Venofer® have been reported in the medical literature.

Treatment-emergent adverse events reported by ≥ 2% of treated patients in the randomized clinical trials, whether or not related to Venofer® administration, are listed by indication in Table 2.

Table 2. Most Common Treatment-Emergent Adverse Events Reported in ≥ 2% of Patients By Clinical Indication (Multidose Safety Population)

Adverse Events (Preferred Term)	HDD-CKD	PDD-CKD	
	Venofer® (N=231) %	Venofer® (N=75) %	EPO Only (N=46) %
Subjects with any adverse event	78.8	72.0	65.2
Eye Disorders			
Conjunctivitis	0.4	2.7	0
Gastrointestinal Disorders			
Abdominal pain NOS*	3.5	4.0	6.5
Constipation	1.3	4.0	6.5
Diarrhea NOS	5.2	8.0	4.3
Dysgeusia	0.9	0	0
Nausea	14.7	5.3	4.3
Vomiting NOS	9.1	8.0	2.2
General Disorders and Administration Site Conditions			
Asthenia	2.2	2.7	0
Chest pain	6.1	2.7	0
Edema NOS	0.4	0	2.2
Fatigue	1.7	0	4.3
Feeling abnormal	3.0	0	0
Peripheral edema	2.6	5.3	10.9
Pyrexia	3.0	1.3	0
Infections and Infestations			
Catheter site infection	0	4.0	8.7
Nasopharyngitis	0.9	2.7	2.2
Peritoneal infection	0	8.0	10.9
Sinusitis NOS	0	4.0	0
Upper respiratory tract infection NOS	1.3	2.7	2.2
Urinary tract infection NOS	0.4	1.3	2.2
Injury, Poisoning and Procedural Complications			
Graft complication	9.5	0	0
Investigations			
Cardiac murmur NOS	0.4	0	0
Fecal occult blood positive	0	2.7	4.3
Metabolism and Nutrition Disorders			
Fluid overload	3.0	1.3	0
Hyperglycemia NOS	0	0	2.2
Hypoglycemia NOS	0.4	4.0	0
Musculoskeletal and Connective Tissue Disorders			
Arthralgia	3.5	4.0	4.3
Arthritis NOS	0	0	4.3
Back pain	2.2	1.3	4.3
Muscle cramp	29.4	2.7	0
Myalgia	0	1.3	0
Pain in extremity	5.6	2.7	6.5
Nervous System Disorders			
Dizziness	6.5	1.3	4.3
Headache	12.6	4.0	0
Hypoesthesia	0	0	4.3
Respiratory, Thoracic and Mediastinal Disorders			
Cough	3.0	1.3	0
Dyspnea	3.5	1.3	2.2
Nasal congestion	0	1.3	0
Pharyngitis	0.4	6.7	0
Skin and Subcutaneous Tissue Disorders			
Pruritus	3.9	2.7	0
Rash NOS	0.4	0	2.2
Vascular Disorders			
Hypertension NOS	6.5	8.0	6.5
Hypotension NOS	39.4	2.7	2.2

*NOS=Not otherwise specified

Treatment-emergent adverse events reported in ≥ 2% of patients by dose group are shown in Table 3.

Table 3. Most Common Treatment-Emergent Adverse Events Reported in ≥ 2% of Patients by Dose Group (Multidose Safety Population)

Adverse Events (Preferred Term)	HDD-CKD	PDD-CKD
	100 mg (N=231) %	300 mg for 2 doses followed by 400 mg for 1 dose (N=75) %
Subjects with any adverse event	78.8	72.0
Eye Disorders		
Conjunctivitis	0.4	2.7
Gastrointestinal Disorders		
Abdominal pain NOS*	3.5	4.0
Constipation	1.3	4.0
Diarrhea NOS	5.2	8.0
Dysgeusia	0.9	0
Nausea	14.7	5.3
Vomiting NOS	9.1	8.0
General Disorders and Administration Site Conditions		
Asthenia	2.2	2.7
Chest pain	6.1	2.7
Edema NOS	0.4	0
Fatigue	1.7	0
Feeling abnormal	3.0	0
Peripheral edema	2.6	5.3
Pyrexia	3.0	1.3
Infections and Infestations		
Catheter site infection	0	4.0
Nasopharyngitis	0.9	2.7
Peritoneal infection	0	8.0
Sinusitis NOS	0	4
Upper respiratory tract infection	1.3	2.7
Injury, Poisoning and Procedural Complications		
Graft complication	9.5	0
Investigations		
Cardiac murmur NOS	0.4	0
Fecal occult blood positive	0	2.7
Metabolism and Nutrition Disorders		
Fluid overload	3.0	3
Hypoglycemia NOS	0.4	4.0
Musculoskeletal and Connective Tissue Disorders		
Arthralgia	3.5	4.0
Back pain	2.2	1.3
Muscle cramp	29.4	2.7
Myalgia	0	1.3
Pain in extremity	5.6	2.7
Nervous System Disorders		
Dizziness	6.5	1.3
Headache	12.6	4.0
Respiratory, Thoracic and Mediastinal Disorders		
Cough	3.0	1.3
Dyspnea	3.5	1.3
Pharyngitis	0.4	6.7
Skin and Subcutaneous Tissue Disorders		
Pruritus	3.9	2.7
Vascular Disorders		
Hypertension NOS	6.5	8.0
Hypotension NOS	39.4	2.7

*NOS=Not otherwise specifiedDrug related adverse events reported by ≥ 2% of Venofer® (iron sucrose injection, USP) treated patients are shown by dose group in Table 4.

Table 4. Most Common Adverse Events Related to Study Drug Reported in ≥ 2% of Patients by Dose Group (Multidose Safety Population)

Adverse Events (Preferred Term)	HDD-CKD	PDD-CKD
	100 mg (N=231) %	300 mg for 2 doses followed by 400 mg for 1 dose (N=75) %
Subjects with any adverse event	14.7	10.7
Gastrointestinal Disorders		
Diarrhea NOS*	0.9	2.7
Dysgeusia	0.9	0
Nausea	1.7	1.3
Vascular Disorders		
Hypotension NOS	5.2	0

*NOS=Not otherwise specified

Adverse Events Observed in Hemodialysis Dependent Chronic Kidney Disease (HDD-CKD) Patients

Adverse reactions, whether or not related to Venofer® administration, reported by >5% of treated patients from a total of 231 patients in the 3 pivotal HDD-CKD Studies were as follows: hypotension (39.4%), muscle cramps (29.4%), nausea (14.7%), headache (12.6%), graft complications (9.5%), vomiting (9.1%), dizziness (6.5%), hypertension (6.5%), chest pain (6.1%), and diarrhea (5.2%).

In the first post-marketing safety study, 665 chronic hemodialysis patients were treated with Venofer® doses of 100 mg at each dialysis session for up to 10 consecutive dialysis sessions for their iron deficiency or on a weekly basis for 10 weeks for maintenance of iron stores. In this study, 72% of the patients received up to 10 doses, 27% received between 11-30 doses, and 1% received 40 to 50 doses of Venofer®. Serious adverse events and drug-related non-serious adverse events were collected. In the second post-marketing safety study, 386 hemodialysis patients were exposed to a single dose of Venofer® (100 mg IV by slow injection over 2 minutes or 200 mg IV by slow injection over 5 minutes). Adverse events reported by > 1% of 1,051 treated patients were: cardiac failure congestive, sepsis NOS and dysgeusia.

Adverse Events Observed in Peritoneal Dialysis Dependent-Chronic Kidney Disease (PDD-CKD) Patients

In the pivotal study of 121 treated PDD-CKD patients, 75 patients were exposed to Venofer®. Adverse events, whether or not related to Venofer® reported by ≥ 5% of these patients are as follows: diarrhea, peritoneal infection, vomiting, hypertension, pharyngitis, peripheral edema and nausea.

In these 75 patients exposed to Venofer®, 9 patients experienced serious adverse events as follows: peritoneal infection (2 patients) and 1 patient each with cardiopulmonary arrest, myocardial infarction, upper respiratory infection NOS, anemia, gangrene, hypovolemia and tuberculosis. None of these events were considered drug-related. Two Venofer® patients experienced a moderate hypersensitivity/allergic reaction (rash or swelling/itching) during the study.

The only drug related adverse reaction to Venofer® administration reported by ≥ 2% of patients was diarrhea.

Three patients in the Venofer® study group discontinued study treatment due to adverse events (cardiopulmonary arrest, peritonitis and myocardial infarction, hypertension) which were considered to be not drug-related.

Hypersensitivity Reactions: See **WARNINGS** and **PRECAUTIONS.**

In clinical studies, several patients experienced hypersensitivity reactions presenting with wheezing, dyspnea, hypotension, rashes, or pruritus. Serious episodes of hypotension occurred in 2 patients treated with Venofer® at a dose of 500 mg.

The post-marketing spontaneous reporting system includes reports of patients who experienced serious or life-threatening reactions (anaphylactic shock, loss of consciousness or collapse, bronchospasm with dyspnea, or convulsion) associated with Venofer® administration.

One hundred thirty (11%) of the 1,151 patients evaluated in the 4 U.S. trials in HDD-CKD patients (studies A, B and the two post marketing studies) had prior other intravenous iron therapy and were reported to be intolerant (defined as precluding further use of that iron product). When these patients were treated with Venofer® there were no occurrences of adverse events that precluded further use of Venofer®.

OVERDOSAGE

Dosages of Venofer® (iron sucrose injection, USP) in excess of iron needs may lead to accumulation of iron in storage sites leading to hemosiderosis. Periodic monitoring of iron parameters such as serum ferritin and transferrin saturation may assist in recognizing iron accumulation. Venofer® should not be administered to patients with iron overload and should be discontinued when serum ferritin levels equal or exceed established guidelines [1]. Particular caution should be exercised to avoid iron overload where anemia unresponsive to treatment has been incorrectly diagnosed as iron deficiency anemia.

Symptoms associated with overdosage or infusing Venofer® too rapidly included hypotension, dyspnea, headache, vomiting, nausea, dizziness, joint aches, paresthesia, abdominal and muscle pain, edema, and cardiovascular collapse. Most symptoms have been successfully treated with IV fluids, hydrocortisone, and/or antihistamines. Infusing the solution as recommended or at a slower rate may also alleviate symptoms.

Preclinical Data:

Single IV doses of Venofer® at 150 mg iron/kg in mice (about 3 times the recommended maximum human dose on a body surface area basis) and 100 mg iron/kg in rats (about 8 times the recommended maximum human dose on a body surface area basis) were lethal.

The symptoms of acute toxicity were sedation, hypoactivity, pale eyes, and bleeding in the gastrointestinal tract and lungs.

DOSAGE AND ADMINISTRATION

The dosage of Venofer® is expressed in terms of mg of elemental iron. Each mL contains 20 mg of elemental iron.

Most CKD patients will require a minimum cumulative repletion dose of 1,000 mg of elemental iron, administered over sequential sessions, to achieve a favorable hemoglobin response and to replenish iron stores (ferritin, TSAT). Hemodialysis patients may continue to require therapy with Venofer® or other intravenous iron preparations at the lowest dose necessary to maintain target levels of hemoglobin, and laboratory parameters of iron storage within acceptable limits.

Administration: Venofer® must only be administered intravenously either by slow injection or by infusion.

Recommended Adult Dosage:

Hemodialysis Dependent-Chronic Kidney Disease Patients (HDD-CKD): Venofer® may be administered undiluted as a 100 mg slow intravenous injection over 2 to 5 minutes or as an infusion of 100 mg, diluted in a maximum of 100 mL of 0.9% NaCl over a period of at least 15 minutes per consecutive hemodialysis session for a total cumulative dose of 1,000 mg.

Peritoneal Dialysis Dependent-Chronic Kidney Disease Patients (PDD-CKD):

Venofer® is administered as a total cumulative dose of 1,000 mg in 3 divided doses, given by slow intravenous infusion, within a 28 day period: 2 infusions of 300 mg over 1.5 hours 14 days apart followed by one 400 mg infusion over 2.5 hours 14 days later. The Venofer® dose should be diluted in a maximum of 250 mL of 0.9% NaCl.

Rx Only

REFERENCE: [1] National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Anemia of Chronic Kidney Disease, 2000. *Am J Kidney Dis.* 37: S182-S238, (suppl 1) 2001.

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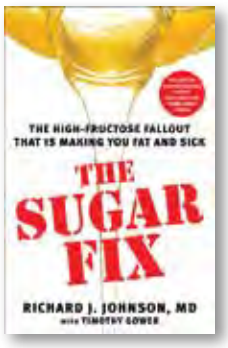
Practice Pointers

In this month's issue, ASN Kidney News *editorial board member Edgar Lerma interviewed Richard J. Johnson, MD, Temple Hoyne Buell and NKF of Colorado Endowed Professor of Medicine, and chief, division of renal diseases and hypertension at the University of Colorado, Denver, about his recently published book* "The Sugar Fix: The High-Fructose Fallout That's Making you Fat and Sick."



Your book, "The Sugar Fix: The High-Fructose Fallout That's Making You Fat and Sick," was recently published. It appears that your book is intended for a lay audience. Do you think that it would still be useful for health care providers, especially nephrologists?

Yes, it is written scientifically and quotes lots of studies, but it is geared for a lay audience that does not know medical language. I think there is something there for everyone.

How did you develop this interest in fructose?

We were aware that the administration of fructose could cause metabolic syndrome in rats. We also knew that mice lacking endothelial nitric oxide also develop features of metabolic syndrome. Finally, we knew that fructose raises uric acid levels, and that raising uric acid in the rat could induce endothelial dysfunction. Thus, we decided to test whether or not uric acid might have a role in fructose-induced metabolic syndrome.

What is the link between fructose and kidney disease, hypertension, and diabetes?

Fructose appears to induce kidney disease, hypertension, and metabolic syndrome via specific metabolic effects that are independent of energy intake, as these syndromes are not observed in rats fed the same amount of glucose. We believe this is due to the unique ability of fructose to cause ATP depletion and uric acid generation within the cell. In turn, raising intracellular uric acid results in a rise in serum uric acid and also induces intracellular oxidative stress, inhibits nitric oxide, and activates inflammatory and vasoconstrictive pathways.

Aside from what we already know about the link between uric acid and kidney disease (gouty nephropathy, chronic tubulointerstitial nephritis, etc.), what new associations has your research discovered?

There are more than 3500 articles to date showing a strong relationship between uric acid and obesity, heart disease, hypertension, stroke, kidney disease, and other conditions. In fact, a number of studies have confirmed that people with elevated serum uric acid are at risk for high blood pressure, even if they otherwise appear to be perfectly healthy.

Uric acid levels among Americans have risen significantly since the early half of the 20th century. In the 1920s, average uric acid levels were about 3.5 mL/dL. By 1980, average uric acid levels had climbed into the range of 6.0 to 6.5 mL/dL and are probably much higher now.

Our new work is opening new roles for uric acid in metabolic syndrome, obesity, and hypertension. We have also found that fructose ingestion can induce all features of metabolic syndrome, including fatty liver and leptin resistance. Our studies suggest that the metabolic syndrome may be an actual disease.

What are the most common sources of fructose?

The most common sources of fructose are from added sweeteners such as sucrose (which contains 50 percent fructose and 50 percent glucose bound as a disaccharide) and high fructose corn syrup (HFCS) (containing 55 percent fructose and 45 percent glucose as monosaccharides). The major sources of these sweeteners are soft drinks, but certainly desserts, pastries, jellies, fruit drinks, etc., often are loaded with sugar. HFCS is also added to many foods one would not naturally consider sweet, but the amounts added are just enough to provide a slightly sweet taste. Fruits and honey also contain fructose. Most fruits have approximately 8 g of fructose and hence are a relatively minor source; they also contain many good nutrients including vitamin C, antioxidants, potassium, and fiber (Figure 1). Hence, natural fruit ingestion does not increase the risk for metabolic syndrome, whereas this is not true for added sugars and fruit drinks and fruit juices, where the concentration and amount of fructose is higher.

So, is fructose just as bad as glucose? Please discuss the "glycemic index" and "fructose index."

Glucose is not bad unless you are diabetic or severely insulin-resistant, as it is elevations in blood glucose and not dietary glucose that appear to drive obesity and diabetes and its complications. While ingesting glucose or starch stimulates insulin, it is not insulin stimulation that is bad, but rather insulin resistance. Fructose induces insulin resistance, but glucose does not. We have suggested the use of a fructose index, which is much more informative than a glycemic index. The reason the glycemic index correlates with obesity is because one of the principal foods with a high glycemic index is sugar. However, it is the glucose component driving the glycemic index of sugar, but it is the fructose component that is responsible for its metabolic effects.

I commonly encounter this question in my CKD patients: "Is soda bad for my kidneys?" What is your take on recent studies that have focused on this subject matter that have provided contradictory findings?

Today, 55 percent of sweeteners used in food and beverage manufacturing are made from corn, and the number one source of calories in America is soda, in the form of high fructose corn syrup.

Food and beverage manufacturers began switching their sweeteners from sucrose to corn syrup in the 1970s when they discovered that HFCS was not only far cheaper to make, it's about 20 percent sweeter than conventional table sugar that has sucrose.

HFCS contains the same two sugars as sucrose but is more metabolically risky to you, due to its chemical form.

The fructose and the glucose are not bound together in HFCS, as they are in table sugar, so your body doesn't have to break it down. Therefore, the fructose is absorbed immediately, going straight to your liver.

Soda will put on weight, induce fatty liver, and cause insulin resistance. This is normally not a good thing. However, some dialysis patients are cachectic, and stimulating and increasing fat stores in these patients may not be a bad thing. Clearly, for an otherwise healthy individual, avoid excess sugar!

Figure 1. Amount of fructose in various fruits

Fruit	Serving size	Grams of fructose
Lime	1 medium	0
Lemon	1 medium	0.6
Cranberries	1 cup	0.7
Passion fruit	1 medium	0.9
Prune	1 medium	1.2
Apricot	1 medium	1.3
Guava	2 medium	2.2
Date (Deglet Noor style)	1 medium	2.6
Cantaloupe	1/8 of medium melon	2.8
Raspberries	1 cup	3.0
Clementine	1 medium	3.4
Kiwifruit	1 medium	3.4
Blackberries	1 cup	3.5
Star fruit	1 medium	3.6
Cherries, sweet	10	3.8
Strawberries	1 cup	3.8
Cherries, sour	1 cup	4.0
Pineapple	1 slice (3.5" x 0.75")	4.0
Grapefruit, pink or red	1/2 medium	4.3
Boysenberries	1 cup	4.6
Tangerine/mandarin orange	1 medium	4.8
Nectarine	1 medium	5.4
Peach	1 medium	5.9
Orange (navel)	1 medium	6.1
Papaya	1/2 medium	6.3
Honeydew melon	1/8 of medium melon	6.7
Banana	1 medium	7.1
Blueberries	1 cup	7.4
Date (Medjool)	1 medium	7.7
Apple (composite)	1 medium	9.5
Persimmon	1 medium	10.6
Watermelon	1/16 medium	11.3
Pear	1 medium	11.8
Raisins	1/4 cup	12.3
Grapes, seedless (green or red)	1 cup	12.4
Mango	1/2 medium	16.2
Apricots, dried	1 cup	16.4
Figs, dried	1 cup	23.0

CJASN: The Right Decision at the Right Time?

By Arthur Stone

The *Clinical Journal of the American Society of Nephrology* (*CJASN*) published its first issue in July 2006, and it has proven very successful in the relatively short time since its launch. In that time, it has more than doubled its initial impact factor, broadened its subscription base, and attracted a global readership. This success is due in large measure to Editor-in-Chief William C. Bennett and his editorial team, originally consisting of deputy editors Harold I. Feldman, MD, Robert G. Narins, MD, and Mohamed H. Sayegh, MD; Managing Editor Bonnie O'Brien; editorial assistant Margaret Marksthaler; and several associate, international, and liaison editors across the country and around the world.

Dr. Bennett and William Henrich, MD, president of the University of Texas Health Science Center at San Antonio and former member of the ASN Council that discussed the necessity of a clinical journal, give much of the credit to Dr. Narins for assessing member interest and articulating the need for the journal to the Council. Within the ASN Council discussion, debate continued about the need for providing the membership with more clinical research information.

Dr. Henrich recently described the Council's thinking: "No one wanted to do something to detract from *JASN*, though many on the Council saw the need for clinical reviews and updates to help ASN be seen as a leader in clinical nephrology and to be perceived as changing with changes in the field."

Membership surveys and assessments of nephrology clinical journals were conducted "every step of the way" to inform the evolving discussions. Eventually, a majority of the Council agreed that the ASN and its membership would benefit from the establishment of a clinical journal that would complement *JASN*.

Given *JASN*'s strong impact factor rating of 7.5 and *CJASN*'s rising impact factor rating of 4.8 (placing it seventh out of 55 in the urology and nephrology category), it appears the Council made the correct decision. As Dr. Henrich summed it up, "It was the right decision made at the right time to enhance ASN."

Dr. Bennett originally estimated that *CJASN*'s impact factor wouldn't be higher than 3. Based on that estimate, he made a bet with his deputy editors, who said it would be much higher. They were right, and Dr. Bennett paid for it by buying dinner for the editorial team at a high-end restaurant during the 2009 ASN Annual Meeting.

In the initial issue of *CJASN* (1), Dr. Bennett and his deputy editors addressed the "explosion of information" in nephrology and explained that the new journal was created to serve as "a home for this emerging mass of clinical/translational research." In an accompanying editorial, Josephine P. Briggs, MD, then director of the Division of Kidney, Urology, and Hematology in the National Institute of Diabetes and Digestive and Kidney Diseases at the National Institutes of Health, and Thomas H. Hostetter, MD, of the Albert Einstein College of Medicine in New York, described the launch of *CJASN* as a "logical consequence of this growing clinical renal research community (2)."

Indeed, the *CJASN* editors emphasized that "whenever possible, application to managing renal disease will be stressed" and that the journal would "provide special emphasis on hypertension, transplantation, and internal medicine." Asked recently if these original objectives have been achieved, Dr. Bennett said, "We're getting there. At nephrology meetings, there are many citations to *CJASN*. I just returned from a transplantation meeting at which the only nontransplant journal cited was *CJASN*."

Dr. Bennett said that *CJASN* has very good articles in transplantation, but could do more in the area of hypertension. "This would be a good area to go after in future marketing," he said. Dr. Henrich agreed that "evolving issues in hypertension would be fruitful for *CJASN* to pursue" because it ties into clinical nephrology. Although nephrologists complete residency training in internal medicine (unless they are pediatric nephrologists who first train in pediatrics), Dr. Bennett explained that nephrologists focus more on their specialty than primary care medicine. The result is very few internal medicine articles in *CJASN*.

Initially, *CJASN* planned to include a list of "ongoing clinical trials available for patient enrollment," but Dr. Bennett said this idea had become redundant, because information on recruitment for clinical trials is widely available. However, he said, *CJASN* does "publish methods of important clinical trials before the trial is completed."

CJASN's accomplishments include:

- continued growth of original manuscripts, with an increase in the quality of submissions;
- growing worldwide recognition, with more than 50 percent of submissions coming from countries outside the United States;
- transition to a monthly publication in 2009;
- podcasts on *CJASN* articles, including CKD and the Urban Poor for World Kidney Day 2010;
- publication of popular series, such as Moving Points in Nephrology, Presse Rénale, and Controversies in Nephrology; and
- publication of articles focused specifically on clinical education.

Dr. Feldman also outlined the following tasks and challenges for the future:

- improve the journal's ability to address the research community's needs while addressing those of the broader readership;
- participate in and respond to a survey of ASN membership regarding *CJASN*;
- continue to respond, in a timely manner, to reader interest in various features; and
- ensure a smooth transition in *CJASN* leadership.

When asked to identify the highlight of his tenure as editor-in-chief, Dr. Bennett said,

"Personally, fulfillment of Dr. Narins' vision of the need for *CJASN*."

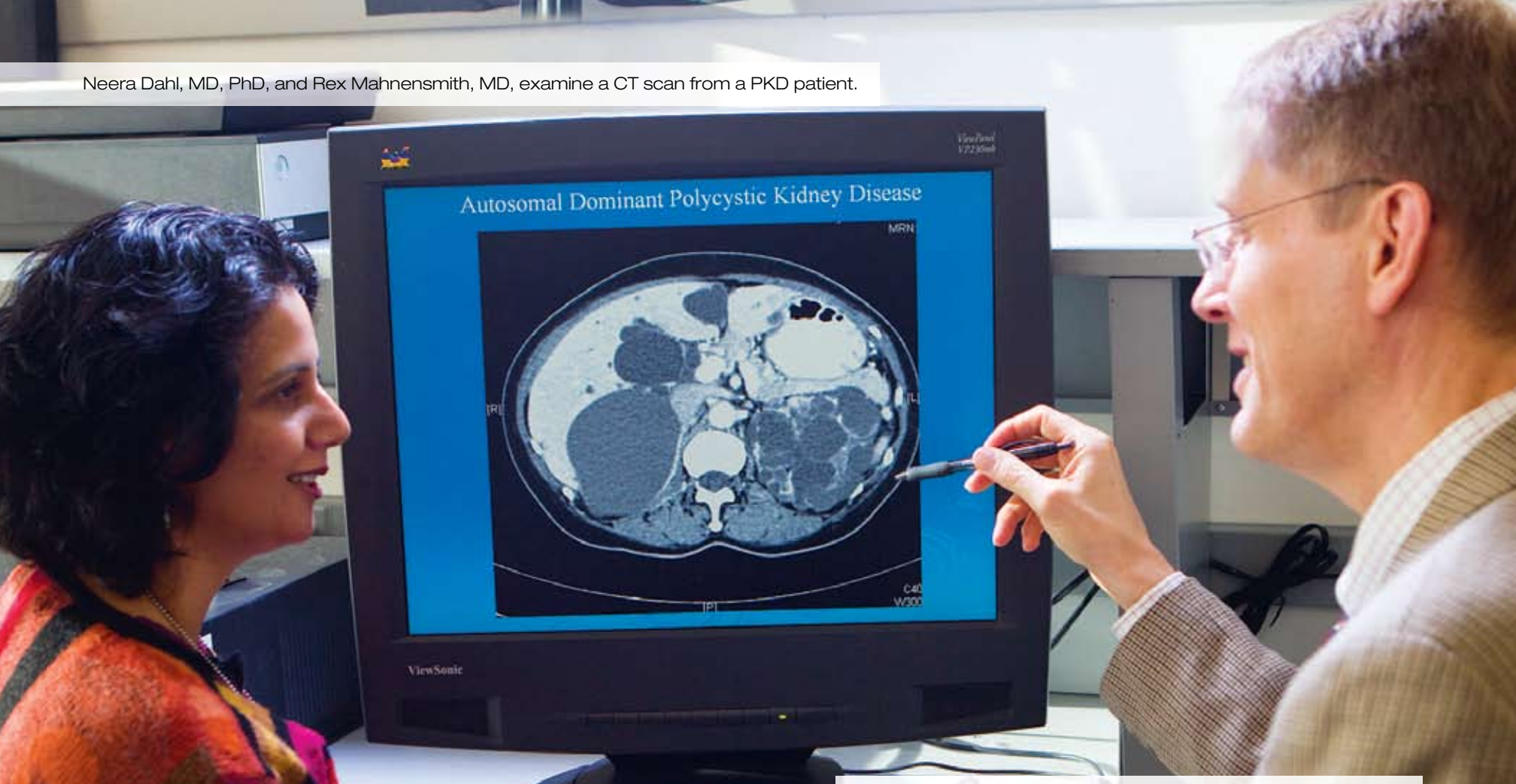
References

1. Bennett W, et al. Dawning of a new ASN journal: satisfying an unmet need in clinical research and education. *Clin J Am Soc Nephrol* 2006; 1:1–2.
2. Briggs JP, Hostetter TH. Opening words for *CJASN*. *Clin J Am Soc Nephrol* 2006; 1:3–5.

Correction

The August *ASN Kidney News* Detective Nephron column included an error in the first column on page 16. Henle's statement at the end of the first column should have read "His primary problem is metabolic alkalosis, and to compensate, his pCO_2 should have been higher." The printed issues incorrectly said ". . . his pCO_2 ahould have been lower."

Also in the first column, Nephron's and Henle's statements starting with "You are both correct and ending with "How so?" belong only on page 17. They were inadvertently also placed on page 16.



Neera Dahl, MD, PhD, and Rex Mahnensmith, MD, examine a CT scan from a PKD patient.

The genetics behind kidney disease are intricate and multi-faceted. Only a few medical institutions in the country have the commitment to understanding and treating inherited kidney diseases and the resources to house the prestigious George M. O'Brien Kidney Research Center and a Polycystic Kidney Disease (PKD) Research Center, all supported by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). We are one of those centers.

Research Excellence, Clinical Leadership and a Commitment to Our Patients

Our researchers have discovered over fifteen genes for human diseases affecting the kidney and blood pressure. These discoveries cover the gamut from rare disorders of blood pressure regulation through sodium and potassium handling such as Liddle's syndrome, pseudohypoaldosteronism type II and Bartter's and Gittelman's syndromes to such common inherited kidney diseases as polycystic kidney disease (PKD). While our researchers are now seeking to translate these findings to treatments for PKD and other disorders, our nephrologists are using these discoveries to help our patients lead healthy and fulfilling lives.

Being at the forefront of clinical research and treatments means that our physicians and surgeons are furthering the current understanding of kidney disease. Most importantly, it means they are positioned to provide the best care possible to our patients.

Yale-New Haven Hospital is the primary teaching hospital of Yale School of Medicine. Kidney disorders services at Yale-New Haven were ranked 33rd by *U.S.News & World Report* in 2010.

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Policy Update

ASN Responds to Proposed HIPAA and Conflict of Interest Changes

In response to a series of recent proposals related to the Health Insurance Portability and Accountability Act (HIPAA) and conflicts of interest (COI) standards and enforcement, the ASN submitted comments aimed at ensuring opportunities for robust and sustained research are protected. The proposed rules suggest changes to existing regulations governing HIPAA and COI. Federal agencies will take into consideration outside commentary (such as that submitted by the ASN) before issuing final rules.

National Institutes of Health Conflicts of Interest

The National Institutes of Health (NIH) has proposed a rule that would alter the way COI are policed at research institutions working with NIH grants. The ASN favors most of the proposals related to institutional COI, including lowering the monetary threshold for a researcher's financial stake to meet the definition of significant financial interest while also supporting public reporting of these interests online. Through written comments, the ASN advocated for uniformity and fairness of COI enforcement across research institutions. The ASN suggested that the NIH develop and disseminate clear guidelines related to administration of COI standards at institutions. Furthermore, a centralized online repository of significant financial interest information would be preferable to each individual institution collecting and posting this information in disparate formats and with varying degrees of timeliness, ASN said in its comments.

Health and Human Services HIPAA

The HIPAA proposed rule relaxes standards for researchers who use data that are covered as protected health information (PHI) under HIPAA. Although the ASN strongly supports PHI, the process of collecting consent forms authorizing its use is burdensome for researchers, institutions, and patients alike.

The first change to HIPAA would eliminate dual consent forms, paving the way for the use of compound authorization forms. Compound authorization would permit use of PHI for both immediate and future research projects while giving patients the choice to opt out.

A second proposal would allow authorizations to cover use of medical specimens in undefined future research activities, typically involving databases or repositories, rather than requiring researchers to specifically cite the intended research purpose at the time of authorization collection.

Finally, the proposed rule would ease rules that bar financial remuneration for preparation and transmission of PHI. If remuneration covers no other expenses, and the intended use of PHI is for research, reimbursement can be provided.

A working group of experts made up of ASN members assisted in crafting the ASN's commentary. Complete comment letters relating to COI and HIPAA are available on the ASN Web site at http://www.asn-online.org/policy_and_public_affairs/medical-research.aspx.

Fate of Midodrine HCl Uncertain

On August 16, 2010, the U.S. Food and Drug Administration (FDA) proposed withdrawing approval for midodrine HCl because the necessary postapproval studies had not been completed. Based on an overwhelming public outcry led in part by the ASN, on September 3, 2010, the FDA took the rare step of rescinding its proposal, thus keeping midodrine HCl available for the time being.

The story began in 1996, when the FDA approved midodrine HCl under an accelerated approval process triggered when a new drug has the ability to treat a serious or life-threatening illness. The drug, developed by Shire Development Inc., was originally approved for use in patients with orthostatic hypotension or low blood pressure. Today, midodrine HCl is used to treat not only orthostatic hypotension but also intradialytic hypotension. The special approval process required manufacturers to undertake postapproval clinical studies exhibiting the drug's clinical benefit. According to an FDA press release, "Since the companies have not been able to provide evidence to confirm the drug's benefit, the FDA is pursuing a withdrawal of the product."

The ASN led the way in advocating for continued approval of midodrine HCl, which according to anecdotal evidence vastly improves quality of life for patients suffering from many diseases related to hypotension. Numerous other physician and patient organizations signed the letter written by the ASN urging the FDA to keep midodrine HCl available to patients. The ASN also wrote a letter detailing the impact of the proposed withdrawal on patients with kidney disease. The drug, which is used to treat patients with orthostatic hypotension and intradialytic hypotension, is an extremely important medication for patients with kidney disease.

"Midodrine HCl is widely recognized among clinicians as the most appropriate, and sometimes the only, treatment option for patients with certain diseases relating to hypotension," said Alfred Cheung, who helped craft the ASN's comments to the FDA. "For example, removing this drug would leave patients and providers with no clear alternative for management of dialysis-related hypotension."

In response to the public outcry, less than three weeks after its initial announcement, the FDA announced that it would allow midodrine HCl to remain available to patients while it addresses legal and regulatory issues related to the drug. The FDA promised to work with Shire Development Inc. as well as the drug's five generic manufacturers to gather the clinical data necessary to support its approval status.

Although midodrine HCl remains on the market, its future is far from certain. The ASN continues to keep a close eye on the outlook for the drug, working to ensure that it remains available to patients with kidney disease while ensuring that the necessary clinical studies are completed to alleviate concerns about its safety. To access the advocacy work the ASN has undertaken on this issue, visit http://www.asn-online.org/policy_and_public_affairs/docs/ASN%20Midodrine%20Letter%20of%20Support.pdf and http://www.asn-online.org/policy_and_public_affairs/docs/Midodrine%20Letter.pdf.

CMS Outlines Potential Quality Measures

The Centers for Medicare and Medicaid Services (CMS) recently released a final report outlining 45 possible future clinical performance measures for end stage renal disease (ESRD) care. The report presents the conclusions of Technical Expert Panels (TEPs) that CMS convened in the spring of 2010 to guide the agency in identifying possible new measures. The report will likely play a role in the selection of future ESRD Quality Improvement Program (QIP) measures as well as other quality programs within the Health and Human Services Department (HHS) and will be of great importance to the renal care community in the coming months and years.

At CMS's invitation, ASN nominated five nephrologists to serve on Clinical Technical Expert Panels (C-TEPs) the agency assembled to provide expertise and input on quality measures pertaining to six specific areas (Table 1). The C-TEP panelists—including the five nominated by ASN—helped define target values for specific current measures. Using the National Quality Forum (NQF) framework, which consists of four criteria—importance, scientific acceptability, feasibility, and usability—C-TEP members identified potential quality measures.

CMS subsequently convened a Data TEP to review the feasibility of collecting the data necessary for calculating the measures and defining the information technology specifications that would be necessary for measure collection. Besides reviewing sources, accuracy, and timeliness of data that would inform these measures, the Data TEP also examined the burden of collection and any practical problems of implementation.

Moving forward, CMS will submit the 45 potential new measures to the NQF for consideration for endorsement in the fall of 2010. The NQF is establishing an ESRD Steering Committee that will study these measures in January 2011; ASN has nominated several expert members to serve on the NQF Committee. The complete CMS TEP report may be located on the ASN patient care website (http://www.asn-online.org/policy_and_public_affairs/patient-care.aspx).

Table 1

Clinical areas considered for quality measure development
1. Anemia management/iron targets (target value for serum ferritin, target value for transferrin saturation)
2. Mineral and bone disorder
3. Hemodialysis vascular access related infections
4. Pediatric hemodialysis adequacy
5. Pediatric anemia (anemia management)
6. Fluid weight management

Table 2

Technical expert Panel	ASN nominees serving on panel
Mineral metabolism	Stuart Sprague, DO, FASN Geoffrey Block, MD, FASN
Vascular access infection rate	Michael Allon, MD
Pediatric anemia	Bradley Warady, MD
Fluid weight management	Rajiv Agarwal, MD, MBBS, FASN

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