ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

Kidney News

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Cystatin C Testing: Should it Be Routine?

By Tracy Hampton

Measuring blood levels of the protein cystatin C can help identify individuals with chronic kidney disease (CKD) who have a poor prognosis, new research finds (Peralta CA, et al. Cystatin C identifies CKD patients at higher risk for complications. *J Am Soc Nephrol*, Janaury 2011).

"The manuscript nicely describes potential methods for incorporation of cystatin C into clinical practice, specifically as a confirmatory test for CKD," said Lesley Stevens, MD, a CKD expert at Tufts University School of Medicine who was not involved with the research.

The findings could impact the care of many patients, because CKD affects millions of adults in the United States, and its prevalence is rising, particularly in the elderly.

Beyond creatinine

To assess kidney function, doctors most often measure an individual's blood levels of creatinine, a breakdown product that is produced by muscles and is filtered by the kidneys. Creatinine tests are imperfect, however, because creatinine levels can vary with muscle mass and protein intake. In addition, creatinine tests cannot accurately detect mild kidney impairment.

"We need a more accurate approach to identifying persons with reduced kidney function. Relying on a serum creatinine test alone leads healthy individuals to erroneously be identified as having chronic kidney disease," said Andrew Rule, MD, of the department of nephrology and hypertension at the Mayo Clinic.

Serum tests of cystatin C, a protein that is filtered from the blood by the kidneys, have emerged as an alternative test of kidney function that

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CKD Children Born Small Have Trouble Catching Up

By Timothy O'Brien

A new study affirms what some pediatric nephrologists already suspected: Children with chronic kidney disease (CKD) who have low birth weight or are born small for gestational age (SGA) may not have the normal "catch-up" growth seen in other children who are born small.

Of course, children with kidney disease are well-known to be at high risk for growth problems.

"But if they're low birth weight or SGA, they're even more likely to have poor growth than other kids with CKD, even correcting for severity of kidney disease, number of years they've had kidney disease, and the type of kidney disease," said Larry Greenbaum, MD, PhD, lead author of the new report. The paper appears in the January 2011 issue of *Clinical Journal of the American Society of Nephrology*.

Based on prospective follow-up in a large sample of children with CKD, the data also show higher than usual rates of low birth weight and SGA birth even in children who do not develop kidney disease until long after birth. "That suggests it's possible that being born low birth weight or SGA may increase the likelihood of developing an acquired kidney disease during childhood," said Greenbaum.

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Inside

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Cystatin C Testing

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is less influenced by muscle mass (see sidebar), p. 4. High cystatin C levels in the blood are indicative of poor kidney function, but cystatin C levels are rarely measured in the clinic.

Cystatin C in CKD

Carmen Peralta, MD, (San Francisco Veterans Affairs Medical Center and University of California, San Francisco) and colleagues studied the potential of measuring cystatin C levels to assess kidney function. Their study included 11,909 participants from the Multi-Ethnic Study of Atherosclerosis (MESA) and the Cardiovascular Health Study, two studies that were designed to investigate various aspects of cardiovascular disease and used standardized measures of kidney function.

"We hoped to illustrate the utility of combining the two filtration markers—creatinine and cystatin C—to refine the diagnosis of CKD," said Peralta. The investigators also looked for any links between cystatin C levels and increased risks for premature death, cardiovascular events, heart failure, and kidney failure—all of which have been linked to CKD.

In MESA, 9 percent of individuals had CKD by a creatinine-based equation only, 2 percent had CKD by a cystatin C-based equation only, and 4 percent had CKD by both equations. In CHS, these percentages were 12 percent, 4 percent, and 13 percent, respectively. Compared with individuals without CKD, individuals in MESA with CKD based on creatinine had only a reduced risk of premature death, whereas individuals with CKD based on cystatin C had more than a threefold increased risk, and individuals with CKD based on both equations had nearly a twofold increased risk.

In the Cardiovascular Health Study, individuals with CKD based on creatinine only had a similar risk of premature death compared with individuals without CKD, whereas individuals with CKD based on cystatin C only had a 1.78-fold increased risk. Individuals with CKD based on both had a 1.74-fold increased risk. The pattern was similar for cardiovascular disease, heart failure, and kidney failure.

These results suggest that among adults diagnosed with CKD using the creatinine-based equation, poor prognosis is limited to patients who also have CKD based on the cystatin C equation. Therefore, cystatin C may have a role in identifying CKD patients who have the highest risk for developing complications.

"Based on our findings, we believe that cystatin C should be a confirmatory test among persons identified as having a creatinine-based estimated glomerular filtration rate below 60 mL/min/1.73 m^2," said Peralta. "Depending on the patient's age, roughly one-third to one-half of these patients will be reassured that they do not in fact have a high risk for CKD complications." Peralta added that although the cystatin C test is infrequently used, it has been approved by the U.S. Food and Drug Administration and is an automated blood test that is potentially available in any hospital laboratory.

"I agree with the approach suggested by Dr. Peralta and colleagues," said Rule. "Both cystatin C and creatinine are influenced by factors other than kidney function. But by using both tests to detect a reduction in kidney function, physicians can better identify persons with chronic kidney disease who are at increased risk for death, heart disease, or the future need for dialysis or a kidney transplant."

Study co-authors include Ronit Katz, DPhil, Ian De Boer, MD, David Siscovick, MD (University of Washington); Mark Sarnak, MD, Andrew Levey, MD (Tufts-New England Medical Center); Joachim Ix, MD (University of California San Diego); Linda Fried, MD (Pittsburgh Veteran's Affairs Medical Center); Walter Palmas, MD (Columbia University); and Michael Shlipak, MD (University of California, San Francisco).

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Kidney News

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Cystatin C Offers Benefits for Certain Patient Populations

Cystatin C is an alternative to creatinine for a filtration marker that has been in use for approximately 25 years. It has been approved as a test in the United States for the past six years, but is rarely used by American nephrologists.

Michael Shlipak of the University of California, San Francisco, noted that a complete changeover to using cystatin C instead of creatinine in the United States would not be practical. But in some clinical situations, a second test—and one that importantly does not change with muscle mass—might be useful, he said. Shlipak spoke at a Renal Week 2010 session on "Cystatin C—Is it time to replace creatinine?"

"If creatinine levels are seen as so important, it's probably worth doing a second test, too, sometimes," he said.

Creatinine levels in the blood are affected by muscle mass, activity level, diet, and health status—in addition to kidney function. Yet only age, sex, race, and weight are considered when calculating an appropriate baseline of creatinine. In contrast, cystatin C is produced in all nucleated cells of the body and is constantly released into the blood, probably due to cell turnover. It is not affected by age, sex, weight, or muscle mass and, by all evidence, it is a better, more linear measure of glomerular filtration rate (GFR), Shlipak said.

A cystatin C test may be particularly useful for populations where muscle mass is unpredictable, such as HIV, liver disease, and cancer patients. HIV patients, for example, have a tenfold higher risk of ESRD, but creatinine levels are not typically elevated in these patients.

In the FRAM study (Fat Redistribution And Metabolism Change in HIV Infection), creatinine levels were the same between groups of HIV patients and age-matched controls, but HIV patients showed a sixfold increase in cystatin C levels. In a five-year follow-up, one-sixth of the mortality risk in HIV patients was found to be attributable to CKD. These data may signal that some proportion of kidney disease in HIV patients is going unrecognized, Schlipak said.

A cystatin C test might also be useful to perform risk stratification for a patient about to undergo a procedure, such as a cardiac revascularization. The TRIBE-AKI study was a prospective study of 1147 patients undergoing cardiac surgery to develop biomarkers that could predict and detect AKI. In this group, cystatin C levels had the most linear relationship with risk of mild AKI compared to creatinine levels or GFR. The findings were not as strong for predicting severe AKI, however.

A cystatin C test could also benefit patients diagnosed with CKD solely from a high creatinine lab result to validate CKD cases. Mortality rates appear to be high in CKD/ESRD patients who have been diagnosed by both the creatinine and cystatin C markers or solely by a cystatin C test, but are lower for patients diagnosed only by a creatinine test or by neither marker.

Finally, Shlipak noted that although there is limited availability for the cystatin C test in hospital labs, two of the three FDA-approved cystatin C tests can now be measured on standard autochemistry analyzers. He said that while many nephrologists will continue to rely on creatinine due to familiarity and lower expense, the test is worth incorporating into practice for these scenarios where the additional test can add power to the diagnosis and monitoring of kidney disease.

When asked if he thought cystatin C was a better test for older patients, Shlipak replied, "I do think it's better in elderly patients because muscle mass becomes more confounding [in this population]."

Low Birth Weight

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Many CKD children are low birth weight or SGA

Greenbaum and colleagues analyzed data on 586 children enrolled in the Chronic Kidney Disease in Children (CKiD) study—a large observational cohort study of children with mild to moderate CKD at 48 North American pediatric nephrology centers. Although the CKiD study was primarily designed to identify risk factors for declining kidney function, assessment of growth failure and related morbidity was an important secondary goal. The final analysis included 426 children: 337 with nonglomerular diagnoses and 89 with glomerular diagnoses.

Based on parental questionnaires, 17 percent of the CKD children had low birth weight (<2500 g)—more than twice as high as reported U.S. population rates. Twelve percent were born premature (gestational age <36 weeks), while 14 percent were SGA (birth weight below the 10th percentile for gestational age).

Forty percent of the sample of CKD children were admitted to the intensive care unit (ICU) immediately after delivery. Neonatal ICU admission was more common in children with nonglomerular diagnoses than glomerular diagnoses (48 versus 9 percent). Otherwise, rates of abnormal birth history were similar between the two diagnostic groups.

Not surprisingly, follow-up data showed a high rate of growth problems, with median age/sex-specific z-scores of –0.73 for height and –0.10 for weight. Among children with nonglomerular diagnoses, those with longer durations of CKD tended to be smaller.

For CKD children born small, it's hard to play "catch up"

To find out how abnormal birth history related to growth, the researchers performed a multivariate repeated-measures analysis. Height and weight z-scores were less than zero even for CKD children with a normal birth history.

However, low birth weight and SGA had negative effects on growth, beyond the impact of CKD. For height, z-score was –0.43 for low birth weight and –0.29 for SGA; the z-scores for weight were –0.37 for low birth weight and –0.41 for SGA.

There was no further effect of prematurity or ICU admission. "Kids who have kidney disease and are born low birth weight or SGA don't seem to grow as well during childhood as the kids who were not low birth weight or SGA, even when you correct for all of the other variables," said Greenbaum.

Using a regression tree approach to evaluate the joint effects of low birth weight, prematurity, and SGA, the researchers distinguished four subgroups with different growth outcomes, based on the number and type of birth abnormalities:

- Zero or one abnormality: average height z-score –0.93
- Low birth weight plus prematurity: average height z-score –1.35
- Low birth weight plus SGA: average height z-score –1.44
- Low birth weight, prematurity, and SGA: average height z-score –1.73

Thus CKD children with all three primary birth exposures had nearly a two-standard deviation reduction in height, with similar effects for children with glomerular and nonglomerular diagnoses. (None of the birth abnormalities affected weight z-scores in children with nonglomerular CKD, although SGA had a "more pronounced" effect in children with glomerular diagnoses.)

"This important paper provides the most compelling evidence to date of something that pediatric nephrologists have noted for some time: that children who start "behind" at birth and have CKD have a much more difficult time growing normally or catching up in growth during early childhood," said John D. Mahan, MD (Nationwide Children's Hospital/ The Ohio State University, Columbus). "It really emphasizes for the clinician the importance of devoting additional time and effort to promoting growth in this specific group of patients."

Richard N. Fine, MD (professor of Pediatrics at Stony Brook University Medical Center) said: "I think that this is an important finding because it indicates that when we see children who are born with or who develop CKD, and who have a history of prematurity or SGA, we should be sensitive to their growth retardation and make concerted efforts to attempt to maximize their growth as they're being treated during the course of CKD."

Think about earlier intervention to promote growth

It's no surprise that CKD adversely affects growth in children. "Children with kidney disease have a variety of potential causes of poor growth," said Greenbaum. "These include acidosis, effects on bone, effects on the function of growth hormone, all of which can make these kids grow poorly."

Taking advantage of long-term follow-up with repeated measures of growth in the CKiD study, the new data lead to some intriguing new insights into the risk and determinants of abnormal growth in pediatric CKD. "Children with CKD who are born small don't seem to have the catch-up growth that other kids that are born small have," Greenbaum said. "And because of that, low birth weight or SGA may be a novel risk factor for poor growth during childhood in children with CKD."

Children who have CKD plus an abnormal birth history could benefit from closer monitoring and earlier intervention for growth problems, Mahan said. "There are things we can do—supplemental feedings, nonglomerular or gastrostomy tubes, growth hormone, for example—that can improve growth in this population of children. And yet the tendency of the care team typically is to give the kid a chance, give the family a chance… 'Maybe he'll catch up if we just watch him a little bit longer.'"

"Most pediatric nephrologists would hopefully intervene for acidosis and bone disease because we follow that very closely," said Greenbaum. "But intervening by doing nutritional intervention or growth hormone is something that we don't do immediately." In the CKiD sample, 14 percent of children received growth hormone: 16 percent of those with nonglomerular diagnoses and 6 percent with glomerular diagnoses. Greenbaum said that's "a relatively low percentage," considering the extent of the growth problems.

According to Mahan, "No one likes to add layers of additional treatment onto a kid with complex medical problems. But an important fact that we need to remember is that normal babies experience about one-third of their statural growth in the first two years of life. "So if the child starts behind because of SGA or prematurity, and then has CKD, that child's going to end up at two years of age further away from where she/he should be based on her/his own genetic heritage. Which means more difficulties catching up during the remainder of childhood."

Children who have CKD plus an abnormal birth history could benefit from closer monitoring and earlier intervention for growth problems.

Could babies born small at birth be at higher risk of CKD?

Meanwhile, the high rate of abnormal birth history in children with acquired kidney disease poses an intriguing new question: Could babies who are born small be at higher risk of developing CKD?

"In the CKiD children, we're seeing an increased incidence of SGA or low birth weight even in children who have acquired kidney disease—which happens much later in life, so it wouldn't instinctively appear to be related to abnormal birth history," Greenbaum said.

"The fact that a history of low birth weight or SGA was also increased in kids with acquired kidney disease suggests that these birth abnormalities might be additional risk factors for the development of CKD," Mahan said. "This is completely in accord with the 'Barker hypothesis' (thrifty hypothesis) suggesting that reduced fetal growth is strongly associated with renal disease. There are similar associations with a number of chronic conditions later in life, such as coronary heart disease, stroke, diabetes, and hypertension. This increased susceptibility is thought to result from adaptations made by the fetus in an environment limited in its supply of nutrients."

Added Fine: "According to the Barker hypothesis, if you are SGA or if you have prematurity, then maybe you have fewer nephrons, and that this may make you more susceptible to development of CKD. This hypothesis has been mostly related to older adults but I think that certainly we need to think about the potential relationship in the pediatric age group."

Although there's no proof of a causal association yet, the CKiD data suggest the adverse health consequences of being born small may start well before adulthood. "Based on our data, this prenatal history of low birth weight and SGA increases the risk of acquiring kidney disease as early as childhood, which no one has ever seen before," according to Greenbaum. "In fact, the associations are stronger in children with acquired kidney disease."

Of course, any risk factor that increases the risk of childhood CKD increases the risk of adult kidney disease. "If they're in the CKiD study, by definition it's a lifelong problem and they're likely to develop kidney failure at some point during life," said Greenbaum.

"We're a long way from advocating any specific recommendations. But I think this study raises the possibility that it may be reasonable to do some monitoring or screening for kidney disease in children or adults who were born low birth weight or SGA."

Fellows Corner

Life After Renal Fellowship: Survey Results

By Deepti Torri, Matthew Sparks, Kellie Calderon, Hitesh Shah, and Kenar Jhaveri

The outlook for securing a job after nephrology training has become increasingly more difficult. A glance at the *New England Journal of Medicine* classifieds shows that the number of jobs advertised for nephrology trainees is decreasing. To assess the current job market for graduating nephrology fellows, we conducted an Internet-based, nine-question anonymous survey.

The survey was created online using SurveyMonkey.com, and a hyperlink was placed on popular nephrology fellow blogging sites such as the Renal Fellow Network (http://www.renalfellow.blogspot.com), Nephron Power (http://www.nephronpower.com), and Uremic Frost (http://www.uremicfrost.com) and the *ASN Kidney News* Facebook Fan page (http://www.facebook.com/ASNKidneyNews) from May 27 to June 25, 2010.

Data were collected anonymously and could only be completed once from a given Internet Protocol address. The respondents were asked about the region of the United States in which their training program was located; whether they were a U.S. citizen or green card holder; whether they were a United States–based university graduate; what their dream job was; whether they had a job position secured for July 2010; if yes, what type of job; and finally, whether they were glad they entered a nephrology training program.

Of the 72 respondents to the survey, 60 were graduating from their respective nephrology training programs (an estimated 17 percent of the total graduating fellow class) (1). Twenty-two (34.4 percent) of the respondents did not have job yet, and five (8.8 percent) were undergoing extra training in nephrology, supporting our hypothesis of the difficult job market. To determine whether or not the respondents were happy with their job selection, we first asked what they considered their dream job to be, then asked what job they were about to start. Interestingly, only two respondents (3.1 percent) initially felt that being a hospitalist was considered their dream job, but six respondents (12 percent) were planning on becoming a hospitalist after completing their training. On the other hand, 16 respondents (25 percent) felt that staying in academia was their dream job, whereas only six (16 percent) planned to stay in academia after completing their training. Twelve respondents (18.5 percent) were not glad that they chose nephrology as career. Table 1 summarizes the responses to the survey.

There are likely several factors contributing to this year's decrease in job opportunities for graduating nephrology trainees. Private practices and academic nephrology groups alike have been affected by recent economic problems. Furthermore, the new bundled payment system that will begin this month and the numerous policy and reimbursement changes enacted this year have likely created some apprehension about hiring new nephrologists. Finally, many groups are opting to hire physician extenders instead of nephrologists in these difficult economic times.

A recent article in *Renal Business Today* reported a phone-based survey in which 104 of 324 graduating fellows indicated that they did not have a job as of May 2010 (2). Likewise, according to the Fellowship and Residency Electronic Database, since 2008 there has been a 50 percent increase in fellows pursuing extra training (2).

In conclusion, our survey results indicate that finding a job within the field of nephrology is difficult. Nephrology positions are available; however, finding the perfect fit for every graduating trainee might prove challenging. We are hopeful that the current job market will improve over the next several years after the economy recovers and the full impact of the bundled payment system plays out.

Several limitations are apparent from this survey. First, our survey was limited by the small sample size of graduating nephrology fellows who responded (60 [17 percent]). Second, the survey was collected anonymously and cumulatively rather than as individual data were available. Furthermore, several questions were not answered by some of the respondents. We were not able to exclude the 12 nongraduating fellows who responded to the survey, which is likely to confound our results. Finally, these results only show a snapshot of the current job market. We can only speculate how respondents would have answered in previous years.

Table 1. Survey questions and answers

Question Asked	Possible Answer	Result (72 total)
1. Are you a June 2010 graduating renal fellow in US-based program?	Yes No	60 (83.3%) 12 (16.7%)
2. In what region of the country is your fellowship program located?	North East West Midwest South	37 (56.9%) 6 (9.4%) 9 (14.1%) 12 (18.8%)
3. Are you an US citizen or Green card holder?	Yes No	46 (71.8%) 19 (29.2%)
4. Are you an American university based medical graduate?	Yes No	26 (40.6%) 38 (59.4%)
5. What is your dream job following graduation of fellowship?	Academia Private practice Hospitalist Combined Hospitalist/ Nephrology practice Extra training (in nephrology/ other disciplines)	16 (25%) 30 (36.9%) 2 (3.1%) 7 (10.9%) 9 (14.1%)
6. Do you have a job position secured following the end of your fellowship? (answer "NO" if you are planning to do extra years of a fellowship)	Yes No	42 (65.6%) 22 (34.4%)
7. If yes to the above question, what WILL YOU BE doing next year?	Academia Private practice Hospitalist Combined Hospitalist/ Nephrology practice Extra training (in nephrology/ other disciplines)	7 (14%) 30 (56.5%) 6 (12%) 2 (4%) 5 (10%)
8. If you are planning to do extra training or fellowship, what is the reason you are pursuing that?	Strictly out of Interest To buy time to look for a job of interest N/A	12 (19.4%) 5 (8.8%) 45 (72.6%)
9. Are you glad you chose nephrology as a career?	Yes No	53 (81.4%) 12 (18.5%)

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Deepti Torri, MD, and Kellie Calderon, MD, are renal fellows at North Shore LIJ Health System. Matthew Sparks, MD, is a renal fellow at Duke University Medical Center. Hitesh Shaw, MD, is the program director for the North Shore/LIJ Health System nephrology fellowship. Kenar Jhaveri is an attending physician at the division of nephrology at North Shore/LIJ Health System.

The List: ASN Kidney News "What to Watch" in 2011

A new calendar year, like a blank page, brings the promise of things to come. *ASN Kidney News* asked the ASN Board of Advisors and attendees at Renal Week 2010 what things the nephrology community should watch in the coming year. We got answers.

Changes to healthcare administration, especially dialysis services, dominated the responses. The Affordable Healthcare Act, bundling of dialysis payments, and the resurrection of CROWNWeb all raise more questions than answers for our community.

The past year brought a prototype implantable kidney and the first bioengineering session at Renal Week. Technological advances clearly form another "thing to watch" in 2011. Renal Week also saw interest in nutrition and kidney problems. Dietary treatment of hypertension and other maladies continues to be of interest in 2011.

Chronic kidney disease prevalence increases with age. As the Baby Boomers hit traditional retirement age this year, the number of older individuals with kidney problems will skyrocket, producing unprecedented interest in aging and the kidney at Renal Week 2010 (as well as a feature section in February's *Kidney News*). This increase in potential patients also raises concern about the nephrology workforce and its potential to meet these patient needs.

Of course, the most important things to watch in 2011 will be those we do not anticipate here. *ASN Kidney News* will keep watching and reporting everything kidney.

Bundled Payments for Kidney Care

By By Jula Inrig , Subodh Saggi, Daniel Weiner, Rachel Shaffer, and Rajnish Mehrotra on behalf of the ASN Dialysis Advisory Group

This month the Centers for Medicare and Medicaid Services (CMS) will implement the most substantial payment reform in the end stage renal disease (ESRD) program since 1983, the new case-mix adjusted bundled prospective payment. Over 90 percent of dialysis units opted to be paid using this system at the outset, but implementation of the bundled payment system will be highly complex, particularly given the absence of evidence-based quality measures for ESRD care. There is a critical need for facile, accurate monitoring of practice trends and patient outcomes that may occur with the impending changes in dialysis care.

Anemia management

The most discussed—and potentially influential—element of the new payment system for 2011 is the inclusion of erythropoiesis stimulating agents (ESAs) and intravenous iron preparations in the bundle. ESAs drive cost variability in dialysis patient care, and have represented a profit source for many dialysis providers for years. Beginning in 2012, two competing forces will affect ESA use: 1) cost of ESAs, and 2) CMS's Quality Incentive Program (QIP), which will financially penalize facilities when patients' hemoglobin levels rise above 12 g/dL or fall below 10 g/dL. Given the inherent variability in hemoglobin levels, maintaining 98 percent of patients within this range will be challenging.

In the absence of data to guide care patterns, providers may accept a substantially larger number of patients with higher hemoglobin levels to meet this target, or reduce ESA dosing across the board, exchanging the financial penalty associated with levels below 10 g/dL for lower costs resulting from less ESA use.

Mineral and bone disorder

Optimal treatment of mineral and bone disorder (MBD) among dialysis patients remains unclear with therapeutic decisions often individualized and frequently based on nephrologists' interpretation of the best available evidence. Effective this month, CMS will include all intravenous (IV) vitamin D preparations and their oral equivalents in the bundle. Oral medications without IV equivalents (most notably cinacalcet and prescription phosphorus binders) will not be included until 2014.

Considering the paucity of data to support the use of one treatment for hyperparathyroidism over another, it is anticipated that use of more expensive vitamin D analogues will decline and that, at least until 2014, there may be preferential use of cinacalcet. Moreover, in response to broad therapeutic ranges for parathyroid hormone, phosphorus, and calcium levels suggested in current KDIGO guidelines, some dialysis organizations have modified protocols to allow higher levels of these parameters—and less medication for MBD management. While treatment decisions should not solely be based on financial considerations, this approach may provide new information about the cost-effectiveness of different MBD agents and therapeutic strategies, assuming appropriate monitoring strategies are in place.

Home dialysis

CMS has long offered incentives to providers intended to increase home dialysis use. The new bundle enhances existing incentives by offering identical payments for home dialysis and in-center hemodialysis. Home dialysis patients use fewer intravenous medications, likely making their care less costly to providers than in-center patients overall. Furthermore, in response to feedback from ASN and others, CMS will pay facilities to train patients for home dialysis (if the training occurs after the first four months after initiating dialysis). These incentives, along with the reimbursement for pre-dialysis education for stage 4 chronic kidney disease CMS has offered since January 2010, may lead to a greater use of home dialysis, particularly peritoneal dialysis.

Nephrologists and dialysis organizations should allocate resources for monitoring their own patients to detect the effects—positive or negative—of the new system.

Patient financial burden

Beneficiaries receiving Medicare Part B services are typically responsible for a 20 percent coinsurance fee. Implementing bundled payments may increase certain patients' financial responsibility. Separately billable medications have always been subject to patient or secondary insurance copayment; so their inclusion in the bundle will not substantially affect patients' financial responsibility. However, some laboratory tests included in the bundle (e.g., blood cultures for dialysis access-related infections) were not formerly subject to copayment. These will represent a new cost to patients—and one unique to the ESRD program.

Because CMS calculated the base bundled payment amount using the average of current costs, patients who are lower utilizers of resources in the current system likely will see increased copayments, while higher utilizers may actually realize a reduction in costs. CMS estimates that the bundled payment system will result in a net 1.2 percent increase in patient copayments, likely varying widely depending on utilization and secondary insurance.

Conclusion

The unprecedented new bundled payment system for dialysis has the potential to improve the quality, delivery, and cost of dialysis patient care. However, in the absence of a demonstration project prior to implementation of the expanded bundle, facile, timely, and effective monitoring will be critical to assess the effects on dialysis quality and patient access. The implementation of CROWNWeb may allow real-time monitoring of changes in dialysis practices and care. However, CROWNWeb will not be fully implemented until later in 2011, and smaller dialysis providers will be unable to batch data, placing them at a disadvantage.

Accordingly, as we embark on this new era of dialysis in the United States, uncertainty remains about CMS' ability to ascertain the effects of bundled payments on issues such as blood transfusions and bone loss and mineral metabolism parameters, as well as patient access to care, including potential disparities based on race/ethnicity or comorbid conditions (cherry-picking). Tracking data on these issues and other outcomes measures will be necessary to ensure the new system is enabling kidney professionals to provide optimum care for their patients.

ASN and the wider nephrology comunity should be encouraged by CMS' openness to input on the bundled payment system to date, and should continue to advocate for the Agency to allocate resources beyond CROWNWeb and the QIP to monitor the effects of the bundle on practice patterns, patient outcomes, and access to care in as close to real-time as possible. Nephrologists and dialysis organizations, too, should allocate resources for monitoring their own patients to detect the effects—positive or negative—of the new system, as well as conducting larger, population-based studies examining dialysis outcomes and practice patterns nationwide.

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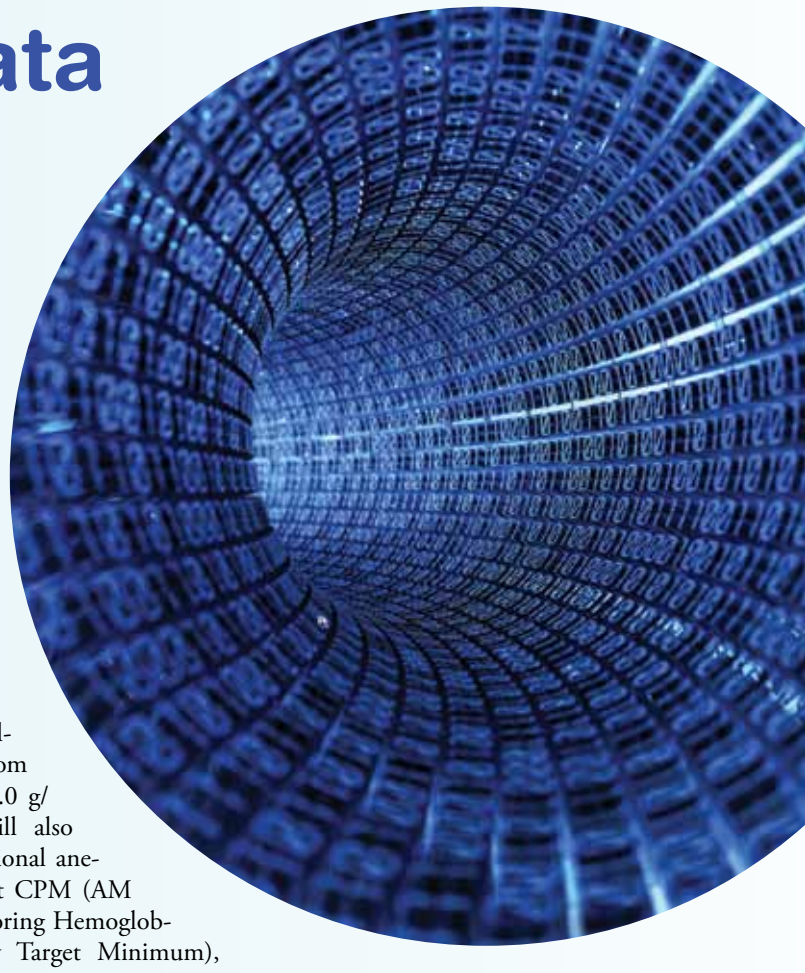
CROWNWeb's ESRD Clinical Performance Measures Data to Be in Place by Mid-2011

By Oniel Delva



A look at how this Web-based data-collection system is intended to help with promoting quality improvement in the renal community.

The Centers for Medicare & Medicaid Services (CMS) in April 2008 announced plans to modernize the way that dialysis facilities report data with the release of CROWNWeb—a system designed to increase the efficiency and quality of data collection for facilities and CMS (1). CMS released the first installment of CROWNWeb to eight Medicare-certified dialysis facilities in February 2009. CMS is currently in the process of moving into the third phase of CROWNWeb's release, which will allow approximately 650 dialysis facilities nationwide to submit their patient and facility data directly to CMS. Once this phase is complete, CROWNWeb will transition into its full national release and will be used by the 5500+ Medicare-certified dialysis facilities in the United States and surrounding territories by mid-2011.

In addition to changing the method by which end stage renal disease (ESRD) facilities report their clinical and administrative data to CMS, the implementation of CROWNWeb will coincide with some changes to CMS' ESRD Clinical Performance Measures (CPM) data requirements. One adjustment is an increase in the percentage of reported patient data to provide a more accurate reflection of patient care needs. The system will also include an adjustment to the mean hemoglobin data collection range to meet current regulations set forth by the U.S. Food and Drug Administration (FDA) regarding dosing recommendations for anemic patients with chronic renal failure, which states dosing should be individualized to achieve and maintain hemoglobin levels within the range of 10 to 12 g/dL (2).

How CROWNWeb works

CROWNWeb is a Web-based data-collection system that allows authorized users to securely submit patient-centric data to CMS from virtually anywhere at any time—with the exception of scheduled downtime for maintenance—as well as to access their facility and patient data for reference purposes. It is the tool designed by CMS to enable facilities to meet the requirements outlined in §494.180(h) of the updated Conditions for Coverage (CfCs) for End-Stage Renal Disease Facilities, published April 15, 2008. This section calls for the electronic submission of administrative and clinical data by all Medicare-certified ESRD dialysis facilities in the United States —a move away from the current paper-based data-collection methods. CMS is leveraging this tool to streamline how the renal community will both report and access facility and patient-centric data. The system will house reports such as the ESRD CPM Reports and Vascular Access Reports, among a variety of others.

Impact on renal community

CROWNWeb's CPM data will serve the same purpose as the traditional ESRD CPM data—to provide a method to monitor the performance of Medicare-certified dialysis facilities on both local and national levels. The system's data will continue to reflect measures based on the National Kidney Foundation Dialysis Outcomes Quality Initiative (NKF DOQI) Clinical Practice Guidelines. However, to provide the renal community with a more accurate reflection of patient care efforts, CROWNWeb's CPM sample (beginning with the full national release) will consist of 100 percent of chronic dialysis patients entered into the system. This is a tremendous increase, as CPM report data have historically been based on a sample comprising only 5 percent to 8 percent of the ESRD total patient population.

In past years, CPM data were only available at the national and Network levels. However, once data on all dialysis patients are reported via CROWNWeb, dialysis units will be able to use the system to generate facility-specific CPM reports. Once fully implemented, CROWNWeb will allow users to view CPM data approximately 45 days after the reporting period ends.

CROWNWeb data for CPMs

Most of the clinical data calculations that will be used with the help of CROWNWeb data will mirror those used during previous ESRD CPM data collection efforts. Modifications have been made to some of the calculations to expand facilities' ability to gauge their patient care efforts, as well as to recognize current regulations by the FDA related to labeling and use of erythropoiesis-stimulating agents (ESAs).

These modifications have resulted in several changes to CPM definitions, most notably to the mean hemoglobin collection range. Historically, the percentage of patients with mean hemoglobin values from 11.0 g/dL to 12.0 g/dL were reported using anemia management CPM I. Now, in an effort to address current FDA guidance, this CPM is defined in CROWNWeb to include patients with mean hemoglobin values ranging from 10.0 g/dL to 12.0 g/dL. Changes will also include an additional anemia management CPM (AM CPM Ib: Monitoring Hemoglobin Levels Below Target Minimum), two vascular access CPMs (VA CPM IIIa: Monitoring and Surveillance of AV Fistula and AV Grafts for Access Dysfunction through Physical Examination; and VA CPM IIIb: Monitoring and Surveillance of AV Fistula and AV Graft for Access Dysfunction through Pre-pump Arterial Pressure), and 12 mineral metabolism CPMs.

The electronic collection and reporting of CPM data via CROWNWeb for all individuals with ESRD will add significant value for facilities as well as for individuals who have or may develop ESRD (3). These benefits include:

1. More timely availability of validation and comparative reports once the data submission is complete, since the CPM data are electronically available.
2. Reduction of lag-time for data collection. CROWNWeb is a dedicated data collection instrument, whereas the primary purpose for claims is for billing rather than quality measurement.
3. Ability for facilities to see facility-specific information that compares them to various peer groups, as the CPM data include all patients and cover all Medicare-certified dialysis facilities.

More information

You can access more information on CROWNWeb by visiting the Project CROWNWeb website at www.projectcrownweb.com, or by visiting the Centers for Medicare & Medicaid Services CROWNWeb website at www.qualitynet.org and clicking on the ESRD tab.

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The author assumes full responsibility for the accuracy and completeness of the ideas presented. The author welcomes comments on the ideas presented; please send comments to CRAFT@ProjectCROWNWeb.org.
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3. Centers for Medicare & Medicaid Services. Conditions for Coverage for End-Stage Renal Disease Facilities; Final Rule. www.cms.hhs.gov/CFCsAndCoPs/downloads/ESRDfinalrule0415.pdf. Apr. 15, 2008: p 74. Accessed Nov. 10, 2010.

The Aging Kidney Will Top Research and Policy Concerns in 2011

The Department of Health and Human Services Administration on Aging estimates that there are currently 39.6 million Americans age 65 or older, representing 13 percent of the population. By 2030, that number is expected to grow to close to 20 percent of the population (http://www.aoa.gov/aoaroot/aging_statistics/index.aspx).

When abstracts containing "elderly" or "aging" were counted for the years 2009 and 2010, each year's Renal Week offered on average 187 abstracts on the topic, compared with an average of 111 for the years 2007–2008. The aging kidney will continue to drive research and policy discussions in 2011.

Concerns about the impact of the aging Baby Boom (202er generation on kidney health care in the coming years were evident as a session on the aging kidney packed a standing-room-only meeting room at Renal Week 2010.

Among the kidney disease implications of our rising elderly population: The most common health condition affecting this population is hypertension. The numbers of patients on the transplant waiting list who are 60–79 years old shot up from around 1500 in 1997 to around 11,500 in 2007. Transplant numbers in this same age group have climbed steadily in the last decade as well.

Lynn Schlanger, a nephrologist at the Emory Clinic in Atlanta, spoke about the changes that take place structurally and functionally in the aging kidney from both animal and human studies. She noted that between the ages of 5 to 59, most people's kidneys do not change in volume, but after that a significant decline in volume occurs.

In aging rats, podocytes hypertrophy, with process effacement and detachment increasing. Another study showed that aging rats have podocytes with increased mass and exhibit glomerular sclerosis as well as proteinuria. In addition, aging kidneys show decreases in the size of cells in the proximal tubules, shortening their length, and an increase in fibrotic activity in the tubulointersitial space.

In a study that took 3D images of kidney vasculature in 31 kidneys from patients ranging from 20 to 79 years of age, changes to arterioles were observed only in persons older than 35. Reviewing other vascular changes, Schlanger said, "All of this suggests that blood vessels changing with age affects the renal mass and [sclerosis] of the glomerulus."

GFR in the aging kidney—benign decline or disease?

Ann O'Hare of the VA Puget Sound Health Care and University of Washington in Seattle, tried to answer "the impossible question" of what is a normal reduction in glomerular filtration rate (GFR) with aging and what signals disease. There is a normal curve that shows a decreasing eGFR with increasing age. Patients such as a 78-year-old man with an eGFR of 15 and a creatinine level of 6 fall well outside this normal aging curve and clearly have kidney disease.

"But what about people close to an eGFR of 60 or less, the cutoff point for disease?" asked O'Hare. "They begin crossing into what is also the normal distribution of eGFR with age."

She cautioned that an eGFR within this normal range does not exclude the possibility of disease in the older population. But it also helps to place ESRD in context for this population. One Kaiser study showed that for patients older than 75, the risk of death is higher than developing ESRD until the point where eGFR reaches a level of 15 or less. A large percentage of patients over the age of 60 with CKD had eGFR levels in the 40–59 range, O'Hare reported, noting this is a range that should alert physicians of older patients.

In cases where the etiology of a low eGFR is uncertain and it falls within the 'normal' range for the patient's age, the physician might be better off switching to an individualized approach rather than a kidney disease approach, O'Hare said. In other words, targeting the patient's preferences and priorities might make more sense, especially in the likely case of co-morbidities, than solely treating them as a CKD patient.

Andrew Levey of Tufts Medical Center in Boston noted that the field is in some ways behind others in thinking about how best to manage aging kidneys and said of a low eGFR, "just because it's common with age, doesn't mean it's benign."

Lynn Schlanger presented her talk, "Pathological Manifestations of an Aging Kidney" and Ann O'Hare presented her talk, "What is a 'Normal Reduction' in GFR with Aging and What is Disease?" in the session "GFR in the Aging Kidney: Benign Decline or Disease?" on Thursday, November 18, at Renal Week 2010.

Bioengineering Advances: Implantable Artificial Kidney Could Do Away With Dialysis

What do individuals with kidney disease think about to pass the countless number of hours they can spend undergoing dialysis treatments? Well, now they may start thinking about a day when dialysis will be a thing of the past.

Researchers last year unveiled a prototype model of the first implantable artificial kidney that could one day eliminate the need for dialysis. Other such advances in bioengineering top the *KN* list of things to watch in 2011.

Recognizing that advances in bioengineering and informatics could have a profound impact on both scientific research and patient care within nephrology, the topics found plenty of interest at Renal Week. Over 80 abstracts from around the world were submitted to the new bioengineering and informatics category.

The implantable artificial kidney is being developed by the University of California, San Francisco's Shuvo Roy, PhD, in collaboration with engineers, biologists, and physicians from across the country. The device, which is about the size of a coffee cup, has been scaled down from a room-sized external model (designed by researchers at the University of Michigan) that works but is much too big for use in patients who need dialysis.

The new system relies on advances in nanotechnology and tissue generation. The implantable model is composed of thousands of nanoscale filters and a BioCartridge of renal tubule cells. Filtration of the blood relies on the body's blood pressure, and the cells reabsorb water, sugars, and salts, as well as produce vitamin D and help maintain proper blood pressure. The technology has been tested in animal models and will soon be ready for clinical trials.

The device is much simpler than a normal functioning kidney, and the investigators do not expect it to replace kidney transplantation; however, it could act as a bridge for patients on transplant waiting lists. Currently, patients are more likely to die on waiting lists than to receive a kidney. More than 85,000 patients are on transplant waiting lists, but only 17,000 donated kidneys were available for transplant last year.

The American Diet and Kidney Disease

Hypertention is the biggest driver of the increased rates of chronic kidney disease (CKD) among Americans. Neither hypertension nor CKD is helped by our obesity epidemic and love of greasy, fried, salty, and sugary foods.

From the first lady's healthy food campaign to some companies' cost incentives for employees to stay thin, food is on our minds. That's why *ASN Kidney News* has chosen food choices and health for our "top to watch in 2011" list.

By 2030, the worldwide population is projected to be 38 percent overweight and 20 percent obese. That's 58 percent of the total population at risk for hypertension and associated kidney complications, said Efrain Reisin, chief of nephrology and hypertension at Louisiana State University Health Sciences Center in New Orleans. Reisin spoke at Renal Week 2010 in Denver in November.

Kidney specialists know the scenario all too well: Visceral fat cells have all of the components of the renin-angiotensin system (RAS), which leads to hypertention-inducing vasoconstriction. These cells also promote chronic inflammation, which induces hypertension as well. Insulin resistance leads to sodium retention and activates the sympathetic nervous system, both playing into hypertension.

Obese, hypertensive patients show a higher escape of albumin than normal weight hypertensives, leading to increased renal blood flow, hyperfiltration, and proteinurea, which results in glomerular injury and eventual CKD or end stage renal disease. In animal studies, glomerular injury and sclerosis in the kidneys has been shown to be caused by a high-fat diet alone.

Hypertension rates are driven not just by increased sodium intake, but also by a decreased potassium intake in the modern Western diet.

"There is growing evidence that it is truly the interaction of the two—sodium and potassium—in the diet that is important, not just their individual levels," said Horacio Adrogué, medical director of dialysis and transplantation at the Methodist Hospital in Houston, Texas.

But how are sodium and potassium interrelated? When blood pressure is plotted against the ratio of Na/K excreted in urine, the higher the ratio, the higher a patient's blood pressure. Also, the higher the potassium intake, the higher a patient's level of aldosterone, which correlates with lower blood pressure. Potassium intake also seems to inhibit sodium sensitivity.

In primitive hunter-gatherer populations the Na/K ratio is about 0.1 compared to a ratio of about 3.0 in the Western diet. In other words, human kidneys evolved to conserve the rare sodium and excrete extra potassium found in the primitive diet. This evolutionary programming of the kidney results today in excess bodily sodium and too little potassium—a combination that leads to hypertension. Adding to the problem is that processed foods are not only higher in sodium, but lower in potassium when compared to fresh foods.

"The most effective, practical advice clinicians can give may be to tell patients to limit the intake of processed foods and eat as much fresh food as possible," said Matthew Weir, director of the nephrology division at the University of Maryland Hospital in Baltimore.

Lowering sodium by just 1.8 g/day leads to a reduction of 5.0 mmHg in blood pressure. It also improves control of hypertension, blunts the age-related increase, increases the effectiveness of antihypertensive medications, and reduces cardiovascular events.

Increased potassium intake lowers blood pressure in everyone, if increased by 50 mmoL/day. But dietary recommendations are lacking for potassium—the Institute of Medicine recommends 120 mmoL/day. But currently, only 10 percent of men and 1 percent of women eat that recommended level.

Reisin, Adrogué and Weir spoke at a "Nutrients and Blood Pressure" session at RenalWeek 2010.

Addressing the Looming Workforce Crisis

Nephrology and geriatrics are the only two internal medicine specialties to attract fewer graduates of U.S. medical schools in 2002 than in 2009. Although the number of nephrology fellowship positions increased, U.S. medical graduates (USMGs) have filled a smaller percentage of them each year (figures 1 and 2) Simultaneously, new legal barriers to immigration have made it increasingly difficult for international medical graduates (IMGs) to train in the United States.

Meanwhile, the chronic kidney disease population continues to burgeon, and demand for providers will grow as 32 million more Americans gain access to health care owing to the Affordable Care Act. As USMG interest in nephrology diminishes—and IMGs face new challenges to practicing nephrology in the United States—the specialty faces a looming workforce crisis. Will there be enough nephrologists to meet the growing demand for kidney specialists?

Recognizing the need to call attention to this crisis, ASN convened a Summit on the Nephrology Workforce during ASN Renal Week 2010. ASN Councilor Bruce A. Molitoris, MD, FASN, presented the recommendations of the ASN Task Force on Increasing Interest in Nephrology Careers (IINC), which he chaired. The task force included nephrology fellows, educators, and other ASN members and was tasked with studying the workforce and developing recommendations for ASN to implement that will increase interest in nephrology careers.

IINC identified more than 30 strategies for increasing interest in nephrology among medical students and residents—as well as women and underrepresented minorities—including enhanced faculty development, teaching tools, mentoring, awards, and kidney disease public awareness efforts. In addition, the task force recommended that ASN help develop creative educational rotations that focus on often overlooked areas in nephrology (such as acute kidney injury, critical care nephrology, hypertension, interventional nephrology, and transplantation). The task force also encouraged ASN to use social media to highlight the positive aspects of nephrology careers.

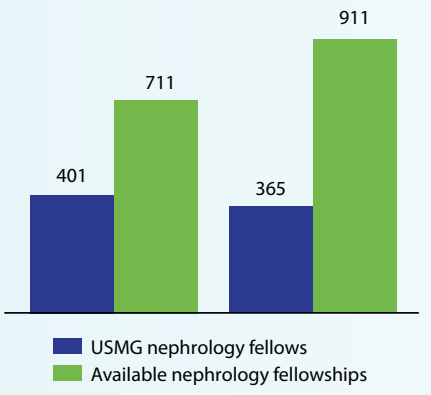
"These sobering data show that we as nephrologists, researchers, educators, and as a professional society, need to take a hard look at how we're presenting nephrology to the public and especially to students today. Increasing public awareness and attracting more new nephrology educators, and as a professional society, need to take a hard look at how we're presenting nephrology to students today," Molitoris said. "Attracting more new physicians and scientists to the specialty is imperative given rising demand for nephrologists, and the time to act is now."

During the Summit on the Nephrology Workforce, Renal Physicians Association (RPA) President Edward R. Jones, MD, summarized the results of the *Young Physicians in Nephrology: 2009 RPA Survey Report*. According to the report, the three main challenges trainees perceive to a career in nephrology are caring for patients in multiple settings, keeping up with clinical advances, and maintaining a work-life balance.

Addressing the crisis in the nephrology workforce will remain at the top of ASN's agenda in 2011. To this end, the society is developing a permanent committee charged with implementing the IINC's detailed recommendations and studying trends in the nephrology workforce over time. Besides convening a follow-up meeting to the 2010 summit during Renal Week 2011, the society will also release an annual report on the state of the nephrology fellowship during the meeting.

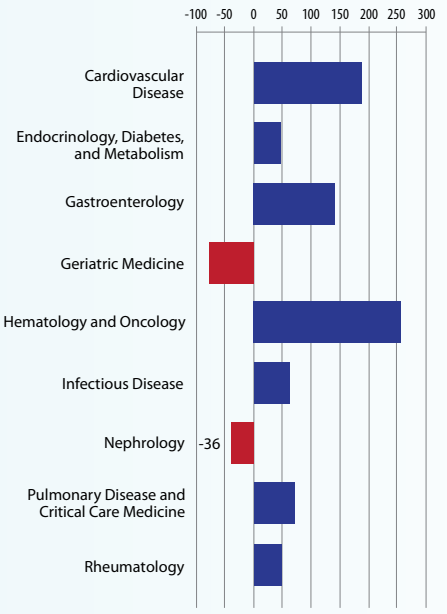
Look for more information on the nephrology workforce and updates on ASN's action to promote the specialty and ensure an adequate number of kidney professionals to meet patients' needs, including a themed issue of *Kidney News* this spring.

Table 1
USMGs entering nephrology vs. number of available nephrology positions



Brotherton SE, Etzel SI. JAMA 2010; 304: 1255-1270
Brotherton SE, Rockney PH, Etzel SI. JAMA 2003; 290: 1197-1202

Table 2
Increase/Decrease of USMGs (2002-2009)



Brotherton SE, Etzel SI. JAMA 2010; 304: 1255-1270
Brotherton SE, Rockney PH, Etzel SI. JAMA 2003; 290: 1197-1202

Policy Update

Congress Compromises to Avoid Drastic Physician Payment Cuts

By Daniel Kochis

In order to temporarily avoid drastic cuts to Medicare physician payments, Congressional leaders agreed to a bipartisan compromise that would maintain the current set of Medicare payments through the end of 2011. While the yearlong "doc fix" is only an interim solution, the compromise allows the incoming Congress time to consider implementing a permanent solution to the flawed Sustainable Growth Rate (SGR), the basis of Medicare physician payments. The SGR has been a recurrent problem for the better part of the past two decades, and ASN has led advocacy efforts to replace it with a new formula that fairly and accurately reimburses physicians for the care they provide.

The federal government implemented the current SGR formula in 1998 to calculate physician reimbursement for the Medicare and Medicaid programs. While the initial formula took into account regional variations as a key predictor in assessing physician reimbursement, today, the data on which annual adjustments are made is no longer current, does not reflect geographic variations, and does not consider the appropriateness of the care provided.

Each year, reimbursement levels calculated by the SGR fall further below the real-life costs of caring for patients—and further below non-Medicare insurance programs' reimbursement rates. Further exacerbating the problem, the SGR does not account for cost increases from new screening programs and expensive new technologies that have proliferated since the SGR was introduced over a decade ago.

The SGR was created to control the growth of health care expenditures by tying physician reimbursement to overall economic growth, but growth in health care expenditures has greatly outpaced economic growth since the beginning of the decade. Consequently, a chasm has opened up between payment cuts called for by the SGR and the real cost of treating patients. As a result of years of temporary delays, a cumulative 25 percent pay cut was scheduled to take effect in January 2011.

While many doctors hoped health care reform legislation would include a permanent fix of the SGR, the bill passed without a permanent solution. The $19.2 billion compromise passed in December 2009 was paid for by changing a tax subsidy program contained within the 2009 health care reform bill. The subsidy pertains to assistance for individuals and families who purchase health insurance.

While the "doc fix" was a welcome reprieve for physicians heading into 2011, Congress will eventually have to find a permanent solution, said ASN Public Policy Board Chair Thomas Hostetter, MD. "If a long term solution is not put into place, the brinksmanship that has characterized the SGR debate may leave some physicians making very difficult decisions, which in turn hurts patients," Hostetter said.

ASN continues to advocate for a permanent fix that respects physician workload and takes into account the best interests of kidney disease patients, and will again bring this message to Congress during ASN Hill Days in the spring of 2011.

CMS to Again Scrutinize ESAs

By Rachel Shaffer

The Centers for Medicare and Medicaid Services (CMS) will meet again on Jan. 19 to study "Erythropoiesis Stimulating Agents (ESAs) for Treatment of Anemia in Adults with CKD Including Patients on Dialysis and Patients not on Dialysis: The Impact of ESA Use on Renal Transplant Graft Survival." As in all previous CMS meetings on ESA use, the American Society of Nephrology (ASN) will again present testimony to the Medicare Evidence Development and Coverage Advisory Committee (MedCAC) panel.

Medicare currently does not have a national coverage determination (NCD) for the use of ESAs for anemia in patients who have CKD. However, over the past year the agency has devoted increased attention to this issue. This month's meeting is the third in a series of Medicare reviews of evidence for ESA use in kidney patients. The Food and Drug Administration (FDA) has also heightened scrutiny of ESAs in recent months (see Table 1).

In March 2010, MedCAC convened a meeting to review the available evidence on the use of ESAs to manage anemia in patients who have CKD. MedCAC's advice can precipitate coverage changes. ASN Public Policy Board member Wolfgang Winkelmayer, MD, ScD, FASN, testified at the meeting that the available evidence shows that current ESAs may be dangerous if used for overly aggressive treatment targets compared with practices that are compatible with current treatment guidelines. Continued access to these medications is required to give patients with CKD a fair chance at receiving and then maintaining a kidney transplant, the society stated, and comparative effectiveness research that closes the evidence gap in the optimal role of ESAs is needed.

CMS did not issue any coverage changes following the March meeting, but in June 2010 initiated a national coverage analysis (NCA) examining evidence regarding the effects of ESAs on health outcomes in adult CKD patients, both pre-dialysis and on dialysis. The purpose of an NCA is to gather input from Medicare, experts, and the public that may influence changes to coverage. NCAs themselves do not change existing policy, but information collected during the course of an NCA could bring about an NCD, depending on the findings. ASN stressed in written testimony for the NCA that any decision the FDA makes regarding ESA treatment for anemia must differentiate among patients with CKD on dialysis and those not on dialysis. Such a decision should also protect patient access to necessary therapies, recognizing the variations in appropriate anemia care in a diverse patient population.

FDA considers ESAs

Meanwhile, the FDA also took a closer look at ESAs. Having instituted a "black box" warning for ESAs in 2009, citing greater risks for death, serious cardiovascular events, and stroke in some ESRD populations, FDA convened a meeting of its Cardiovascular and Renal Drugs Advisory Committee (CRDAC) to discuss the risks and benefits of ESAs in the treatment of anemia in patients with CKD based on the results from the recent Trial to Reduce Cardiovascular Events with Aranesp® Therapy (TREAT), and to potentially consider labeling changes for this patient population in October 2010. ASN again presented testimony, stating that TREAT outcomes support the current label, which is grounded in the best evidence currently available and has been adequate to support individualized treatment decisions among patients and their physicians.

So, what does all this increased attention mean for nephrologists and their patients? One of the primary rationales ASN and others have presented to CMS for preserving CKD patient access to ESAs is the drug's effectiveness in preventing blood transfusions, since transfusions decrease patients' likelihood of receiving or maintaining a transplant due to immune sensitization. On Jan. 19, CMS will take a closer look at the evidence available to support a portion of that position—whether or not ESAs affect transplant survival. The agency appears to be assembling evidence that might allow it to come to a conclusion on the effects and most appropriate use of ESAs for CKD patients, and is methodically narrowing its focus to subsets of that population.

Whether such a conclusion would alter existing labeling and coverage is unknown. For the time being no labeling or coverage changes for ESAs are imminent. The results of the January 2011 meeting will likely provide further insight into CMS' next steps, and CMS is also expected to release a "Decision Memo" for the NCA on March 16, 2011. ASN will continue to advocate for nephrologists and their patients this coming January and in subsequent CMS and FDA examinations of ESAs and other renal care drugs.

Table 1
Timeline of recent CMS and FDA scrutiny of ESAs

March 2010:
MEDCAC reviews available evidence on the use of ESAs to manage anemia in CKD patients

June 2010:
Medicare National Coverage Analysis (NCA) reviews evidence regarding the effects of ESAs on health outcomes in adult CKD patients, both pre-dialysis and on dialysis

October 2010:
FDA CRDAC examines the risks and benefits of ESAs in the treatment of anemia in patients with CKD based on TREAT results

January 2011:
MEDCAC to review evidence of the impact of ESA use on renal transplant graft survival

ASN News

ASN Establishes Strategic Plan to Help Guide Society Through 2016

The American Society of Nephrology (ASN) was founded in 1966 by 18 physicians. The mission they developed for ASN was to foster the exchange of knowledge about nephrology through hosting meetings, supporting science, and working with other societies.

ASN quickly established itself as the premier educational resource in nephrology. ASN Renal Week became, and remains, the most important meeting in kidney research, practice, and education. Over time, ASN launched journals, developed a grants program, added educational offerings such as the Board Review Course and Update and the Nephrology Self-Assessment Program (NephSAP), and developed regional meetings in the United States (Renal WeekEnds) and abroad (ASN Highlights). In recent years, the society has added a career center, a monthly newsmagazine, podcast and video programs, and multiple distance-learning opportunities.

The establishment of the Public Policy Board in 2006 significantly broadened ASN's leadership role in the medical community and among legislators and policymakers. ASN began advocating to improve patient care and to increase funding for kidney-related research. Through policy and advocacy, ASN expanded its influence and reach beyond education, communications and publications, and grants.

When Sharon Anderson, MD, FASN, became ASN President in November 2009, ASN had 11,390 members, funded $3,640,500 in research and travel grants, and hosted nearly 13,000 participants annually at Renal Week. Along with this growth in size and scope, the society faced the most significant economic downturn in decades, major health care reform and changes in kidney care policy, as well as an impending crisis in the nephrology workforce.

Dr. Anderson began a strategic planning process to help ASN leaders determine how the society could continue to serve the interests of its members and the entire kidney community. "No society has endless resources or endless energy," she noted, "and ASN is in danger of going in more directions than it can sustain." Dr. Anderson believed that "ASN needs to develop a clear set of core activities and priorities for the immediate future."

After considerable background work, the members of the ASN Council devoted a three-day meeting in August 2010 to strategic planning. Leaders focused on the society's major areas of endeavor: education, communications and publications, policy, grants, and workforce, and on giving ASN a clear plan for future progress.

The society's leaders first crafted a mission statement to reflect ASN's core commitments and role as a leader in the kidney community:

ASN leads the fight against kidney disease by educating health professionals, sharing new knowledge, advancing research, and advocating the highest quality care for patients.

The leaders then analyzed current and anticipated activities in each of the main areas of ASN endeavor, such as education. Over the course of three days, they developed a strategic plan to ensure that ASN could most effectively support members' interests and address the major challenges facing nephrology (Table 1).

Joseph V. Bonventre, MD, PhD, FASN, succeeded Dr. Anderson as ASN President on Sunday, November 21, 2010. Under Dr. Bonventre's leadership, the society has started to implement elements of the strategic plan. One of Dr. Bonventre's priorities is to lead ASN into a more proactive role in the public forum. "The organization will serve its membership and kidney patients most effectively if the general population learns more about the importance and prevalence of kidney disease."

During Dr. Bonventre's presidency, ASN will also focus on the impending shortage of nephrologists. "It's critically important to get more people interested in working on the kidney and treating patients with kidney disease," he said. "I think we have only scratched the surface in thinking about innovative ways to address that challenge."

In its final report, the ASN Task Force on Increasing Interest in Nephrology Careers recommended several such strategies. For example, the task force encouraged ASN to use social media (including blogs, Facebook, and Twitter) to highlight the positive aspects of nephrology careers. The task force also encouraged ASN to develop creative rotations for medical students and residents that focus on key areas in nephrology, such as interventional nephrology.

ASN's portfolio has expanded dramatically since 1966 to now include policy, grants, and workforce. As stated in its strategic plan, however, the society is still committed to education, communications, and publications. For example, ASN plans to offer a practice improvement module in dialysis in 2011 to help the society's members complete Part IV of the American Board of Internal Medicine's Maintenance of Certification Program.

If you wish to comment on the ASN Strategic Plan (or to volunteer to help implement the plan), please email ASN at ASN@asn-online.org. The society's leadership and staff welcome your feedback, your assistance, and your continued commitment to leading the fight against kidney disease.

Table 1
Five-step plan for accomplishing ASN's mission by 2016

1. Educate health professionals by increasing the value of ASN education. In addition to ensuring that ASN Renal Week remains the premier kidney meeting, ASN will:
   - Provide education (with appropriate credit) for physicians and scientists as well as for doctors of pharmacy, pharmacists, advanced practice nurses, and physician assistants.
   - Disseminate education in as many formats as possible.
   - Develop a mechanism for helping ASN members personalize the society's education to meet their professional needs.

2. Share new knowledge by improving the quality and expanding the reach of ASN's communications. Besides maintaining the premier publications in kidney disease, ASN will:
   - Develop a mechanism for helping ASN members personalize the society's communications to meet their professional needs.
   - Integrate educational material for the public.
   - Raise public awareness of kidney disease.

3. Promote the highest quality care by serving as the professional organization informing health policy in kidney disease. ASN will help its members:
   - Provide expert care to patients.
   - Perform cutting-edge medical research.
   - Educate the next generation of health professionals.
   - Reduce health disparities related to kidney disease.
   - Advocate for increasing awareness of kidney disease within the federal government and among policymakers.

4. Advance patient care and research in kidney disease by strengthening the pipeline of clinicians, researchers, and educators. To accomplish this goal, ASN will:
   - Implement a strategy to increase interest in nephrology careers, which includes promoting diversity within the nephrology workforce.
   - Help fund travel to ASN educational activities for physicians and researchers training in the field of kidney disease.
   - Use the ASN Grants Program to support outstanding research and foster career development.

5. Continue to bolster the ASN infrastructure, which includes:
   - Increasing diversity—including age and experience, ethnicity, and gender—at all levels of the society.
   - Providing avenues for helping ASN members facilitate professional exchange.
   - Expanding ASN membership.
   - Increasing the ASN Council-Designated Endowment Fund (independent of operational budget) to support grants and other priorities.

Dale J. Benos 1950–2010: scientist, teacher, colleague

The renal physiology community suffered a major loss with the sudden death of Dr. Dale J. Benos on October 7, 2010. Dale died while taking a walk with his wife, one week after his 60th birthday. Dale was an active ASN member and was on the first editorial board of the *Journal of the American Society of Nephrology*, serving from 1989–1994. While Dale's research spanned many disciplines, he is best known within the ASN for his seminal studies of renal sodium and chloride transport in the distal nephron. Dale was widely regarded as a teacher and mentor by his trainees. Perhaps even more importantly, he was universally respected as a colleague and genuinely nice person by all who were fortunate enough to have known him. Dale is survived by his wife and two daughters.

Dr. Benos was the Endowed Professor and Chairman of the Department of Physiology and Biophysics at the University of Alabama at Birmingham (UAB). Dale received his BA degree in Biology from Case Western Reserve University and his PhD in Physiology and Pharmacology at Duke. He was an Andrew W. Mellon Scholar in the Laboratory of Human Reproduction and Reproductive Biology at Harvard Medical School. Dale joined the Harvard faculty as Assistant Professor in the Department of Physiology and Biophysics in 1978, and was promoted to Associate Professor in 1983. Dale moved to UAB in 1985. He was appointed Senior Scientist in the Nephrology Research and Training Center at UAB, one of the leading renal research centers in the United States. He was also appointed Senior Research Scientist in the Gregory Fleming James Cystic Fibrosis Research Center, and then in 1987, was appointed full Professor in the Department of Physiology and Biophysics. Dr. Benos became Chair of the Department of Physiology and Biophysics in 1996. Dale subsequently obtained Senior Scientist positions in the UAB Center for AIDS Research, the Comprehensive Cancer Center, the Arthritis and Musculoskeletal Center, and the Center for Computational and Structural Biology. In 2005, Dale was named UAB's first holder of the Endowed Professorship in Physiology.

Dr. Benos' research interests include mechanisms of cation transport across epithelial and cellular membranes. His laboratory frequently presented their work on the molecular biology of sodium and chloride channels from renal epithelia at ASN annual meetings. His work yielded seminal contributions to our understanding of renal ion transport and hypertension. Dr. Benos also made important research contributions into the molecular biology of sodium and chloride channels in lung, trachea, and brain; developmen-

tal aspects of ionic transport and metabolic function in preimplantation mammalian embryos and cultured neural and epithelial cell lines; and pathogenesis of AIDS Dementia Complex. Dr. Benos authored 221 original articles, 87 invited reviews, 10 commentaries, and edited five books. Dale was the Principal Investigator for 19 individual NIH research grants and has a patent pending for research efforts involving inhibition of inward sodium currents in human cancer.

Dr. Benos was widely regarded as a teacher and mentor. Dale taught for several years in the American Physiological Society's Professional Skills Development Course. His efforts went well beyond the weekend program, as he kept in touch with the trainees with whom he worked and continued to offer guidance to them after the course. Dale trained many graduate students and postdoctoral fellows over his career, many of whom went on to highly successful research careers. Dale was also active in medical student education at UAB and played a leading role in developing and revising the curriculum at UAB. Dale was editor of the American Physiological Society's *Physiology in Medicine* series. These papers highlight the physiologic basis and understanding of human diseases. I frequently used these papers on rounds to teach my medical students, residents, and fellows.

Dr. Benos was very active in serving several professional societies, in addition to the ASN. He was most active in the American Physiological Society, where he served as editor-in-chief of the *American Journal of Physiology—Cell Physiology*, Chair of the Publications Committee, and as the 79th President (2006–2007). Dr. Benos also served several other professional societies, including the Council of Science Editors; Society of General Physiologists; American Society for Biochemistry and Molecular Biology; Association of Chairs of Departments of Physiology; Society for Neuroscience; New York Academy of Sciences; the Biophysical Society; and the American Society of Cell Biology. Given Dr. Benos' extensive experience in scientific publications, he was a leader in developing courses addressing ethics in research publication, both at UAB and in the American Physiological Society's Professional Skills Development Course.

On a more personal level, I was privileged to serve on several American Physiological Society committees over the years with Dale. We frequently shared rides to and from the airport, as flights to Birmingham often involve a connection in Atlanta. I took advantage of these rides to learn from Dale and get mentorship and advice on various topics. However, what I remember most fondly was Dale telling me about how happy and proud he was to be coaching his daughters' softball teams. Dale was an accomplished athlete, especially in baseball and softball, and his success in the Birmingham City Softball League was legendary among renal physiologists. Over the past few years, Dale would speak with great pride about his daughters, their softball teams, and his family. Dale will be greatly missed by all who knew him. Our deepest sympathy goes to his family.

Jeff M. Sands, MD, is Juha P. Kokko Professor of Medicine and Physiology, director of the renal division, and executive vice chair of the department of medicine at Emory University in Atlanta.

Industry Spotlight

Phosphate in the News

Vifor Pharma, the pharmaceutical business sector of the Galenica Group, and Fresenius Medical Care (FMC) have announced that they will enhance their current relationship by creating a specialty drug company. The new nephrology company will "develop and commercialize innovative and high quality products to improve the life of patients suffering from chronic kidney disease (CKD) worldwide," according to information from Galenica.

The new company will offer Venofer and Ferinject (or Injectafer, the brand name for Ferinject in the United States) for dialysis and also provide for patients who are considered to be in predialysis condition (CKD stage III to V). The company also will sell PA21, a novel iron-based phosphate binder.

Vifor Pharma, an expert in phosphate binding, is considered a major player in the field of iron replacement therapy. FMC, the world's largest provider of dialysis products and services, will provide access to its network of dialysis centers.

A promising new phosphate-binding drug has reached the final stages of testing for approval from the U.S. Food and Drug Adminstration. According to Bloomberg News, the new drug Zerenex, an experimental therapy from Keryx Pharmaceuticals, requires fewer pills (six to eight per day), an advantage over the Genzyme drugs Renagel and Renvela, which can require up to 10 pills per day per patient.The phase III trial of 146 subjects tested three doses of Zerenex for 28 days and found that the two higher doses – six and eight pills per day – lowered phosphate levels by 25 percent and 29 percent, respectively, according to the company. This therapy worked at a 6-g/day dose. The 1-g/day arm did not show statistical significance, according to a report in Bioworld.

New Erythropoietin Drug Shows Promise—with Reservations

A promising new drug may help bodies release red blood cell growth factor, which would be a boon to dialysis patients. In a phase I trial of this drug, known as FG-2216, researchers found that plasma erythropoietin (EPO) levels rose from 13 to 31 times after one dose. The trial was conducted in 12 patients on dialysis and six healthy individuals.

MedPage Today cautioned that the study was "unable to demonstrate that the drug's effect on EPO was durable enough to reduce clinical anemia or to document its safety with repeated dosing."

With that caveat, the study did show promising results, even in a subgroup of six patients on dialysis who had no kidneys. The results question the concept that dialysis-related anemia occurs in patients with weakened kidneys who can no longer make their own EPO.

"Our results confirm that both the liver and the kidneys retain significant production capacity for erythropoietin in end stage renal disease patients," wrote lead researcher Wanja M. Bernhardt, MD, of Friedrich Alexander University in Erlangen, Germany, and colleagues in the *Journal of the American Society of Nephrology*.

FG-2216 stimulated EPO production in dialysis patients whose kidneys had been surgically removed to treat cancer or other conditions. The increase in EPO production in patients without kidneys was almost as high as in people with normally functioning kidneys. In the patients without kidneys, FG-2216 apparently stimulated production of EPO by the liver.

In the trial, a 20-mg/kg dose of FG-2216 was given to six dialysis patients whose kidneys had been removed, six dialysis patients with severely dysfunctional kidneys, and six individuals with normal kidney function and no other major illnesses.

Of the 12 participants with kidneys, all but one showed maximal effects of EPO 12 hours after dosing, according to the study authors.

FG-2216 is not the only drug in development at this time for this purpose. "Many compounds are in development for this purpose, but this is the only one that has resulted in a published paper in humans," said Volker H. Haase, MD, Vanderbilt University Medical Center Nashville in an interview in *Medscape Medical News*. "Other agents are in phase 2 clinical trials also."

Hasse noted that the drug targets hypoxia-inducing factors (HIFs), and warned that HIF is a complex transcription factor that could have downstream effects on iron metabolism and cell growth and differentiation, for example. "It is important to consider the potential side effects of molecules that target this pathway, and it is too early to say whether this is going to be a successful therapy or not," he told Medscape.

Top 10 reasons to join ASN

ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

1. Lead the fight against kidney disease
2. Receive the finest kidney journals, publications, and e-communications
3. Earn CME credits and MOC points to keep your credentials current
4. Reduce your registration fees for ASN educational programs
5. Submit abstracts for presentation at ASN Renal Week
6. Advocate for patients and the providers who care for them
7. Apply for research grants and travel support
8. Strengthen the community through service on ASN committees
9. Use the ASN Career Center to find a new job or hire the right person
10. Gain FASN status to reflect your expertise, achievement, and commitment

Join or renew
ASN membership online at www.asn-online.org/membership

Journal View

Lower Blood Pressure Target Doesn't Reduce Kidney Disease Progression

In patients with hypertensive chronic kidney disease (CKD), intensive blood pressure control does not affect the risk of progressive kidney disease except in patients with baseline proteinuria, according to a report in *The New England Journal of Medicine*.

In the African American Study of Kidney Disease and Hypertension (AASK), 1094 black patients with hypertensive CKD were randomly assigned to intensive versus standard blood pressure control. Mean arterial pressure targets were 92 mmHg and 102 to 107 mmHg, respectively. During a subsequent cohort phase, the blood pressure target was 130/80 mmHg. The rate of CKD progression— defined as doubling of serum creatinine, diagnosis of end stage renal disease, or death—was assessed at up to 12.2 years' follow-up.

During the trial phase, mean blood pressure was lower for patients in the intensive-control group (130/78 versus 141/86 mmHg). During the cohort phase, both groups had blood pressure readings near the 130/80 mmHg target. In the overall study population, there was no difference in the risk of progressive CKD at either time.

However, there was a significant interaction between group assignment and baseline proteinuria. Among patients with a protein-to-creatinine ratio >0.22, intensive blood pressure control was associated with an approximately 25 percent reduction in the risk of progression (hazard ratio 0.73).

Observational studies show a "direct and progressive" relationship between blood pressure and the risk of CKD progression. The AASK trial evaluated the benefits of intensive blood pressure control among black patients, a group at high risk of hypertensive CKD.

In the overall AASK population, intensive blood pressure control did not reduce the risk of CKD progression. However, the investigators concluded that "in the subgroup of patients with baseline proteinuria, a lower blood-pressure target may significantly reduce the risk of progressive CKD." These findings have implications for current guidelines recommending more intensive blood pressure reduction in patients with hypertensive CKD [Appel LJ, et al. Intensive blood-pressure control in hypertensive chronic kidney disease. *N Engl J Med* 2010; 363: 918–929].

Biomarkers in Glomerular Diseases

Biomarkers, usually proteins measured in the urine or blood, could help nephrologists identify and track glomerular diseases without the need for a kidney biopsy or serial biopsies. Such markers might also be able to predict prognosis of a disease, predict a patient's response to certain therapies, and even guide the choice of therapy as a disease progresses.

John Arthur and his laboratory at the Medical University of South Carolina in Charleston have been working to identify proteins that could specifically identify different glomerular diseases, such as focal segmental glomerulosclerosis (FSGS), lupus nephritis, membranous nephropathy, and diabetic nephropathy.

They first asked whether different patterns of proteins present in urine could distinguish between the different disease states. They ran samples of patients' urinary proteins through two-dimensional gel electrophoresis, which separates the samples first by the protein electric charge in one direction, and then by protein size in another direction.

From this, the team found that "several proteins were statistically different between groups of patients, but none of them had the characteristics to be good markers." The team then asked whether the full patterns of the proteins could accurately predict which disease patients had. In a small sample size, their software program accurately picked FSGS for three of four FSGS patients, but for diabetic nephropathy patients the program picked correctly only half the time.

The method clearly needs improvement, but Arthur noted that "the physiological rationale is there because the specific differences in the glomerular basement membrane that determine what proteins get let through are related to the different electric charges on proteins."

Lupus nephritis diagnosis and classification is also currently done by renal biopsy. In testing whether previously identified markers such as interferon γ-induced protein 10 (IP-10), the IP-10 receptor, transforming growth factor γ, vascular endothelial growth factor, β1 integrin, and cytokines were useful at predicting the class category of lupus nephritis patients, Arthur's group found none of them to be powerful enough.

"But what about predicting a lupus flare with a urine or blood test?" Arthur asked. "That could guide the timing of treatment and allow us to better treat patients." Again, there are several candidates, including neutrophil gelatinase-associated lipocalin (NGAL), interleukin-6, vascular cell adhesion molecule-1, and forkhead box P3. In a study of 111 patients and multiple observations, higher levels of urinary NGAL appeared to show up one month before patients experienced a flare. "This needs to be followed up further, but it is very interesting data," Arthur said.

He also presented data showing that urinary CD-80 might serve as a marker of minimal change disease (MCD), noting that MCD relapse patients have higher levels of CD-80 compared to both MCD patients in remission and FSGS patients. Finally, he reviewed a small study that hints that liver fatty acid binding protein could be a marker of membranous nephropathy. In addition, another study found that 70 percent of patients with membranous nephropathy had an antibody to the phospholipid A2 receptor present in their blood.

"In summary, biomarker research is really in its infancy in glomerular diseases and the availability of clinical samples is a major impediment–none of these potential biomarker candidates have been validated by large numbers of patient samples," Arthur cautioned.

Index to Advertisers

ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

ASN Membership

Member Benefits

Education

ASN provides member discounts for a variety of exceptional educational activities:

- **Renal WeekEnds 2011** summarize, critique, and integrate key Renal Week 2010 presentations in powerful two-day courses (presented in four locations across the United States).
- **16th Annual Board Review Course and Update** prepares nephrologists for the ABIM initial certification and maintenance of certification examinations and provides a comprehensive update for the practicing nephrologist.
- **ASN Renal Week 2011** remains the world's premier gathering of kidney professionals presenting advances in treatment, research, and education.

Abstract Submission allows members to submit and sponsor abstracts for oral and poster presentation at ASN Renal Week.

ASN In-Training Examination for Nephrology Fellows helps identify gaps in training and is similar in design to the ABIM certifying examination.

Online Geriatric Nephrology Curriculum provides essential education in geriatric nephrology.

Grants & Funding

ASN funds more than $3 million annually for research and travel grants.

Membership Services

ASN supports several initiatives to enhance members' careers:

Membership Directory
Access ASN member contact information through a searchable online directory.

ASN Committees and Advisory Groups
Volunteer to serve on an ASN committee and help guide the future direction of the society.

ASN Career Center
Advertise jobs, review candidates, post resumes, apply for positions, and reach employers and recruiters—all through one website.

Fellows of the American Society of Nephrology (FASN)
Achieve FASN status and have your outstanding credentials, achievements, and scholarship recognized.

Policy and Public Affairs

Stay informed about how current and future legislation affects nephrology and improve treatment, research, and education by volunteering to help ASN advocate on behalf of members and their patients.

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Receive all ASN publications and communications in print and online:

Journal of the American Society of Nephrology (JASN)
The leading kidney journal in the world.

Clinical Journal of the American Society of Nephrology (CJASN)
The primary resource for cutting edge clinical research in nephrology.

Nephrology Self-Assesment Program (NephSAP)
An essential tool for earning continuing medical education credits and maintenance of certification points.

ASN Kidney News
A news magazine offering exceptional coverage of current issues of interest to kidney professionals.

ASN Kidney News Podcasts
A bi-monthly audio program providing in-depth discussions of topics that interest and challenge the global kidney community.

ASN Kidney Daily
A daily email collating kidney-related news from medical journals, newspapers, and other media.

ASN Social Media
Connect, engage, and stay informed through the ASN Facebook, Twitter, and YouTube sites.

Member Categories

Active Member ($295)

An individual who holds an MD, a PhD, or the equivalent, resides in North or Central America, and fulfills at least one of the following criteria:

- Completion of research or clinical training in nephrology.
- Specialized training in nephrology during residency or other relevant postgraduate education.
- Publication of at least one peer-reviewed paper in nephrology.
- Experience as a specialist in kidney disease and related conditions.

Corresponding Member ($295)

An individual who meets the criteria for active membership but resides outside North or Central America.

Affliate Member ($295)

An individual in nephrology or allied fields who is not eligible for Active or Corresponding membership.

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WIN provides access to senior women in the field of nephrology who mentor more junior physicians and scientists. **Please note that WIN membership is separate from ASN membership.**

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A senior member retired from clinical, research, and teaching activities who wants to receive print and online subscriptions to ASN publications.

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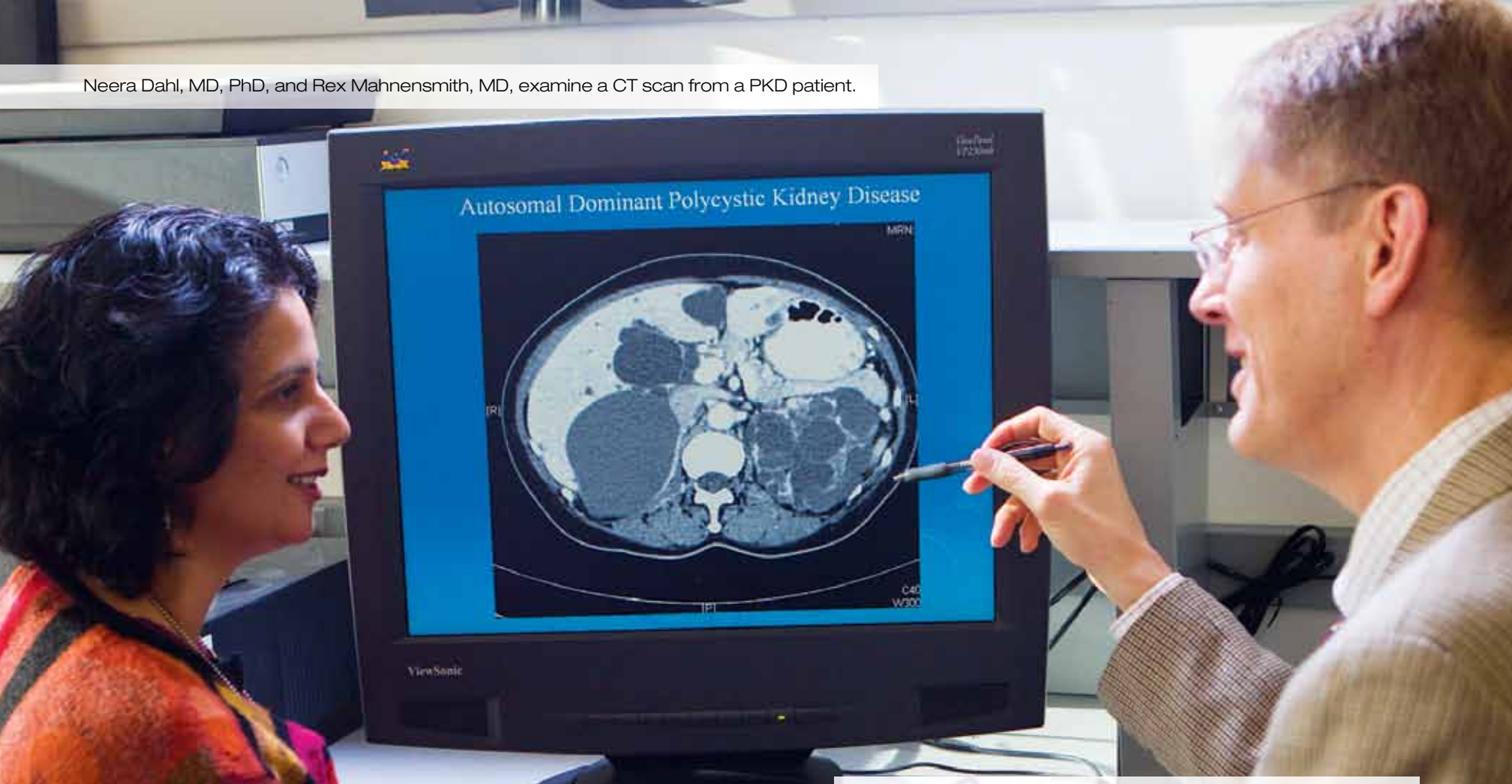
Join or Renew ASN membership online at www.asn-online.org/membership/

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



Research Excellence, Clinical Leadership and a Commitment 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.

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.

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

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