Fatigue may be Life-Threatening for Some Dialysis Patients

By Tracy Hampton

Undergoing dialysis may not be a physically strenuous activity, but dialysis patients with end stage renal disease experience profound levels of fatigue. While physicians may be aware that fatigue is a debilitating symptom experienced by patients undergoing dialysis, there is only limited information on its prevalence and its association with patient outcomes.


Can Fatigue Be Fatal?

Although fatigue has been reported to affect from 60 percent to 97 percent of chronic dialysis patients, it may be the last thing on nephrologists’ minds as they monitor and treat patients’ other potentially life-threatening complications. Concerns about kidney failure, malnutrition, increased risks of cardiovascular disease and death, and other dangers are more pressing among kidney specialists. However, some have suspected that fatigue may not be as innocuous as once thought.

“It is my experience that patients have different interactions with dialysis and that substantial numbers of patients are washed out after treatments,” said Mark Unruh, MD, of the University of Pittsburgh Medical Center. "Profound fatigue may not..."

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Reimbursements May Drop for Some Dialysis Facilities under Bundled Payments

Researchers Voice Concern about High-Poverty Areas of South

By Timothy O’Brien

When it comes to the financial impact of the proposed ESRD bundled payment system, all dialysis centers may not be created equal. A study presented at Renal Week 2009 suggested that dialysis units with certain characteristics and in some regions—including some of the most impoverished regions in the United States—could see disproportionate cuts in Medicare payments under the new system.

Under a bundled payment system, Medicare makes a single reimbursement for all the hospital and physician care for kidney disease, rather than separate payments for the facility and physicians.

“Based on facility-level analysis, it appears there may be unanticipated geographic variation in facility reimbursement payments,” according to lead author Sumit Mohan, MD, of Columbia University. The findings raise concerns that some dialysis centers—and the patients they serve—may be at risk under the Centers for Medicare & Medicaid Services’ (CMS) proposed Medicare bundle.

Continued on page 4
Before you start, stop.

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Renvela® (sevelamer carbonate) tablets or for oral suspension is an effective first-line monotherapy for controlling serum phosphorus in dialysis patients—without calcium or metal accumulation. Renvela is the only phosphate binder available in both tablet and powder dosing options.

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only interfere with daily activities, but it may also influence adherence to the medical regimen. If true, this could have serious consequences for patients' health.

Unruh and his colleagues set out to determine the effects of fatigue on dialysis patients by examining the correlates of self-reported fatigue at initiation of dialysis and after one year. They found that fatigue was associated with health-related quality of life and survival in 917 dialysis patients. Patients in the study were a subpopulation of participants in the Choices for Healthy Outcomes in Caring for End-Stage Renal Disease (CHOICE) Study, a national prospective cohort study of incident hemodialysis and peritoneal dialysis patients that enrolled patients from 1995 to 1998.

Unruh and his colleagues assessed the extent to which fatigue was associated with health-related quality of life and survival in 917 dialysis patients. They assessed the extent to which fatigue was associated with health-related quality of life and survival in 917 dialysis patients. The researchers found that the average vitality score of these end stage renal disease patients was similar to that of patients with clinical depression. A low vitality score was independently associated with white race, higher Index of Coexistent Disease score, higher body mass index, physical exercise, antidepressant use, and higher C-reactive protein (CRP) levels. A lower vitality score was strongly associated with lower SF-36 physical functioning, mental health, bodily pain scores, and decreased sleep quality (all p <0.001) at baseline.

Also, among surviving participants in the study, higher serum creatinine at baseline was associated with preserved vitality at one year (Adjusted Odds Ratio 0.84; 95 percent Confidence Interval 0.72–0.98, p = 0.03). Patients with the highest baseline vitality scores experienced longer survival (hazard ratio 0.79; 95 percent confidence interval 0.58–0.96, p = 0.03).

The researchers also analyzed the effect of change in vitality over one year on survival. The median survival for those with a decline in vitality at one year was 3 years, compared with 3.8 years for those with stable or improved vitality. Also, compared with patients who reported stable or improved vitality at one year, patients who reported a decline in vitality had a 41 percent increased risk of death (HR 1.41; 95 percent confidence interval 1.06–1.89, p = 0.02) after adjusting for age, sex, race, use of antidepressants, dialysis modality, albumin, creatinine, and other factors.

The investigators speculate that the existence of a pathogenic inflammatory factor common to fatigue and decreased survival may explain these findings.

Fighting Fatigue

Kidney researchers not involved with this study noted that the link between low vitality scores and an increased risk of premature death could be important, but it must be verified with additional studies. "In an epidemiological study such as this, causality cannot be proven," said Srinivasan Beddhu, MD, associate professor of medicine at the University of Utah Health Sciences Center in Salt Lake City. "But this is a very important first step, and interventions that improve sleep quality or increased physical activity might improve vitality scores and survival."

They also noted that the observed differences in survival among different types of patients on dialysis are intriguing. "A very interesting finding is that nonwhite race was associated with higher adjusted vitality scores," said Alan Kliger, MD, clinical professor of medicine at Yale University School of Medicine in New Haven and past president of the Renal Physicians Association. "African Americans report more vitality and less loss of vitality than non-African Americans, so race appears to impact adaptation to dialysis. It's not surprising that sociologic and economic factors impact adaptation to disease, but this finding deserves further study."

Fatigue is clearly important to patients. Most—94 percent—of the dialysis patients surveyed would accept more frequent hemodialysis if it would increase their energy. Certain steps can...
Variations by Dialysis Center Ownership

Mohan, along with co-authors William McClellan, MD (Emory University School of Medicine) and Rich Murell, MBA, MA (Amgen), retrospectively analyzed data from all U.S. dialysis centers, drawn from CMS and other federal sources. Their goal was to identify the geographical characteristics of dialysis centers at risk of reduced payments under the proposed bundled payment system.

Their initial study looked at the impact of the model developed by the Kidney Epidemiology and Cost Center (KECC) at the University of Michigan, commissioned by CMS. KECC estimated that, based on ownership characteristics, some types of dialysis facilities would be more likely to see reduced reimbursements—specifically, large dialysis organizations (LDOs), defined as corporations owning 100 or more freestanding dialysis units located in more than one region and hospital-based dialysis units. “We used the KECC estimates for our model, which found about a 0.9 percent reduction for the LDOs and an average 1.6 percent reduction for hospital-based dialysis units,” said Mohan.

The prospect of reduced payments to hospital-based dialysis units raised special concerns because these centers tend to be a safety net for patients who might otherwise face difficulties accessing dialysis services, according to Mohan. “They tend to have a larger percentage of uninsured patients or they tend to be geographically isolated units,” he said.

However, when the researchers ran the analysis using the preliminary estimates issued in September by CMS using a slightly different payment model, a different picture emerged. Under the revised CMS plan, LDOs take an even bigger hit. “It’s now a 3.7 percent reduction for the LDOs, i.e., the three largest chains in the country,” said Mohan. Meanwhile, the CMS proposal seems to reverse the projected drop in reimbursements forecast under the original KECC model. “The hospital-based units actually gained somewhere in the range of 3.7 to 4.0 percent.”

Unanticipated Geographic Variation Raises Concerns

Geography appears to be another factor affecting the likelihood of reduced reimbursements under the ESRD payment bundle. “Our facility-level analysis suggested considerable geographic variation in the impact of the bundled payments on facilities across the country, with adversely impacted facilities being predominantly in the South,” said Mohan. Their original analysis based on the KECC model suggested that dialysis centers located in the South and Southeast—virtually all of ESRD Network regions 5, 6, 7, and 8—were at risk of reduced payments forecast under the original CMS plan, LDOs take an even bigger hit. “It’s now a 3.7 percent reduction for the LDOs, i.e., the three largest chains in the country,” said Mohan. Meanwhile, the CMS proposal seems to reverse the projected drop in reimbursements forecast under the original KECC model. “The hospital-based units actually gained somewhere in the range of 3.7 to 4.0 percent.”

The Congressional mandate to CMS included the requirement to use some type of geographical weighage, Murell explained. “Any first analysis based on KECC facility characteristics used census region for that geographic weightage. That is how we saw such stark results in certain geographic areas. It was when we modeled the CMS data using a wage index refined to a lower level of geography—specifically, the Core-Based Statistical Area (CBSA)—that we saw the similarities between low wage index areas and poverty.”

“The areas that have a low wage index are relatively poor and are also the areas that have facilities that get hit with lower reimbursement rates,” said Mohan. “If you actually look at the wage index map, it almost superimposes on a poverty map. And most of the poverty in the United States is in the South and Southeast.”

This echoes concerns about reduced access to pre-ESRD care in the same areas. Previous research led by McClellan—published earlier this year in Journal of the American Society of Nephrology (2009; 20:1078–1085)—found geographic clusters of suboptimal care for patients with advanced chronic kidney disease in the South and Southeast. The result was that patients in these areas were less likely to receive recommended pre-ESRD care, which in turn led to poorer survival after starting dialysis.

McClellan emphasized that the disproportionate effects on underserved regions and patients are unintended consequences of both the original KECC model and the subsequent CMS proposal. “This is just a consequence of the tools that they had to use to come up with a case-mix adjustment rate that met their revenue adjustment goals,” he said.

Reduced Reimbursement for High-Quality Care?

The quality of dialysis care provided in high-poverty areas has emerged as another interesting piece of the puzzle. “When we compared dialysis facilities most likely to be at risk of lower reimbursements, we found they performed better than the rest of the country on CMS’s quality metrics for adequacy and achieving hemoglobin concentrations above 10 g/dL,” said Mohan. “And yet, under the CMS proposal, the facilities that you’re going to take money away from, disproportionately.”

Prompted by these findings, one of McClellan’s students, Eiichiro Kanda, MD, matched data from the previous study on pre-ESRD care to the new data on facility characteristics of care. “As we found previously, the care prior to going to the dialysis center was heavily influenced by the poverty of the community, and that tended to cluster in high-poverty areas,” said McClellan. “However, once patients got into that dialysis center, their care was no longer influenced by the area of poverty.” (Kanda also presented his research at Renal Week 2009.)

Thus poverty in the surrounding
community is much less likely to affect the center-to-center variability in care, as opposed to pre-ESRD care. “CMS has done a pretty good job at removing some of the impact of poverty after patients get into the system,” said McClellan.

**Call for a More Sophisticated Approach**

McClellan added, “Quite apart from the pros and cons of establishing rates and bundling services as cost containment measures, we would hope that the geographic consequences, particularly as they impact disadvantaged populations—the very populations CMS is committed to bringing more equitable health care—would be examined in a more sophisticated manner than they have been to this date.”

Some of the ownership and geographic variations go hand in hand, reflecting differences in the way dialysis services are provided in different parts of the country. “The genesis of all this work was simply putting all the dialysis facilities on the map and seeing where they clustered geographically,” said Muttell. “When we did that, we saw in the North how it’s dominated almost by hospitals, while other areas of the country are pockets where the medium dialysis organizations operate.”

A more nuanced approach to reimbursement would consider local differences in dialysis care, according to Muttell. “The point of looking at the impact of location is that when you try to apply something universally across the board and don’t take into account these rather unique regional and geographical characteristics, it could lead to some of these unanticipated consequences that I’m seeing.”

The researchers found some other important differences in their updated analysis of the proposed CMS bundle, compared to the original analysis based on the KECC model. “When the original KECC analysis was done, the geographic factor that was supplied to us was at the census region level, where we saw some of those bigger swings,” said Muttell. “In the follow-up analysis, we’re looking at a more granular wage index area.”

The updated analysis showed differences in how the states were ordered in terms of their percentage of dialysis centers at risk of reduced reimbursements—including a less consistently negative impact on the states in the South and Southeast. “More states now have a net statewide loss,” Mohan said. “The average reimbursement per state will be lower, and far fewer states will show a gain. But what states are in what category has switched around quite a bit.”

Other effects of the CMS proposal include eliminating disincentives to peri- toneal dialysis and home dialysis. Several other critical issues remain to be worked out, such as the impact of policies regarding Medicare Part D drugs. Mohan and colleagues believe their findings have important implications for the final CMS bundle. At press time, the researchers were working to prepare a summary of their findings before the scheduled end of the CMS comment period in mid-December.

The aggregation of high-poverty areas in the Southeast deserves special consideration in designing the final bundle plan, McClellan said. “If government policies for health care reimbursement shortchange those poor communities, then it may have consequences that we’d rather avoid—especially since, as seems to be the case, some of the things that have been done in the U.S. dialysis system may actually be benefiting those populations.

The system is capable of getting beyond the poverty issues and poor education to providing decent care for everybody, which I think is a goal that everybody, no matter where they fall on the health care reform debate, would strive for, and that’s equitable, high quality care—for everybody.”

The researchers don’t claim to have “the truth or the answer” to the best ESRD payment bundle, McClellan added. “What we’re doing is holding a mirror up to this process and letting CMS see it as we see it. And asking them, Is this picture accurate, and does it depict what you really want to see from your policy initiatives? And if we get them thinking about it, it will really be a major accomplishment.”

Fatigue

**Continued from page 3**

be taken to counteract fatigue in dialysis patients who are fatigued. “Physicians should screen dialysis patients for fatigue that interferes with quality of life and daily activities,” Unruh said. “In addition, they should ascertain if there are addressable causes of fatigue in the patient such as sleep disorders, mood disorders, hypothryroidism, and polypathy.”

A better understanding of the interactions between factors such as type of dialysis, sleep, depression, and cytokine production may help clinicians develop interventions to improve survival and quality of life among dialysis patients, Unruh said.

“The authors identify several potential avenues for intervention, including increased levels of physical activity,” said Nancy Kuttner, PhD, director of the United States Renal Data System’s Rehabilitation and Quality of Life Special Studies Center and professor in the department of rehabilitation medicine at Emory University in Atlanta. “And although the etiology of fatigue is likely multifactorial, addressing depression may be a valuable intervention at least in a subset of patients.”

In addition, “clinicians and patients might speculate about inflammation, which correlates with both fatigue and survival.” Kliger said. “Could techniques that reduce both fatigue and survival improve both?”

Clinical trials are in the works to address many of the unanswered questions about dialysis and fatigue. An ancillary study in the Frequent Hemodialysis Network Trial supported by the National Institutes of Health (Kidney Int 2007; 71(4):349–359) is examining the impact of dialysis on sleep and fatigue.

ASN News

**ASN: What’s in a Name (or a Logo)?**

Members of the American Society of Nephrology (ASN) dedicate countless hours and myriad talents to improving the lives of millions of patients worldwide who live with kidney disease. Since the society’s inception in 1966, ASN leaders and staff have supported this dedication by advancing professional education, advocating for research support, and promoting ever higher standards of care for patients.

In 2008, ASN leaders hired a leading health care communications firm, GYMR, to survey members, staff, external partners, and other stakeholders to better understand how the society is perceived by kidney professionals. Responses to a 52-question survey and numerous interviews were very consistent: ASN was considered the premier professional society supporting intellectually rigorous kidney education and research, was regarded as a successful and highly credible organization, and was known for holding the world’s most essential meeting focused on kidney disease (ASN Renal Week). Many respondents, however, were unaware of how active a role ASN plays in addressing current concerns in kidney disease and policy.

Society leaders recognized that if ASN were to continue to build on its work advancing health care and science, the society must more accurately reflect the strength and energy members and leaders bring to improving all aspects of kidney health. To better highlight ASN’s role in promoting improvements in clinical care, research, education, and health care policy, ASN leaders began to evaluate how the society presents its goals, agendas, and achievements. ASN contracted with a leading design firm, Informatics, to develop a new logo and visual identity. Leaders agreed that the logo and identity should embody ASN’s active role in the kidney community.

The society tagline, “Leading the fight against kidney disease,” introduced in 2009, recognizes the effort, passion, and results ASN members bring to addressing health care challenges. Staff and leaders continue to highlight the dynamic role ASN and its members play in educating professional stakeholders, shaping policy, extending key partnerships, and advocating for the best in kidney care. As part of this ongoing effort, ASN will introduce a new logo on January 1, 2010, that reflects the creativity, strength, and dedication that has always marked the achievements of ASN and its members.

This logo will serve as a tangible symbol of ASN’s commitment to leading the fight against kidney disease as well as to improving lives through kidney care, research, and education.
s-ORETHANOFANEMIC#+$PATIENTSHAVEIRONDElCIENCY

Guidelines recommend monitoring ferritin and hemoglobin as early as 3-6 months. Regular monitoring of ferritin and hemoglobin along with hemoglobin is a critical part of optimal anemia management.

References:
More than 50% of anemic CKD patients have iron deficiency

KDOQI™ guidelines recommend monitoring TSAT, ferritin, and hemoglobin as early as CKD Stage 3

Regular monitoring of TSAT and ferritin along with hemoglobin is a critical part of optimal anemia management
Get it write

Proven results

- PhosLo® (calcium acetate) achieved KDOQI target levels for mean serum phosphorus and Ca x P product within 3 weeks in a 8-week CARE study.1

- No significant difference in the progression of coronary artery calcification following equivalent lipid control in the PhosLo and sevelamer treated groups in CARE-2 study.2

- No mortality benefits with sevelamer when compared to calcium-based phosphate binders in DCOR (Genzyme-sponsored) study.3

- No mortality, morbidity, or hospitalization benefits with sevelamer over calcium-based binders as stated in DOOR secondary analysis.4

Proven consistency

- Well tolerated with limited GI side effects5
- Not associated with metabolic acidosis6
- Nearly two decades of proven results

PhosLo is indicated for control of hyperphosphatemia in end-stage renal failure. Patients with higher-than-normal serum calcium levels should be closely monitored and their dose adjusted or terminated to bring levels to normal. PhosLo is contraindicated in patients with hypercalcemia. No other calcium supplements should be given concurrently with PhosLo. Nausea, hypercalcemia and priapism have been reported during PhosLo therapy.

Please see brief summary of prescribing information and references below. For more information on PhosLo, please contact Fresenius Medical Care at 888-321-1418 or visit phoslomed.com


BRIEF SUMMARY OF PRESCRIBING INFORMATION

CONTRAINDICATIONS: Patients with hypercalcemia. INDICATIONS AND USAGE: For the control of hyperphosphatemia in end-stage renal failure. WARNINGS: Patients with end-stage renal failure may develop hyperphosphatemia when given calcium with dialysis. No other calcium supplements should be given concurrently with PhosLo. Progressive hyperphosphatemia due to the increase in PhosLo may lead to severe or to require emergency measures. Chronic hyperphosphatemia may lead to metabolic acidosis, and other soft-tissue calcification. The serum calcium level should be monitored twice weekly during the early dose adjustment period. The serum calcium times phosphate (Ca x P) product should not be allowed to exceed 55. Radiographic evaluation of affected skeletal regions may be helpful in early detection of soft-tissue calcification.

PRECAUTIONS: Excessive dosage results in hypercalcemia; therefore, early in the treatment during dosage adjustment, serum calcium should be determined twice weekly. Should hypercalcemia develop, the dosage should be reduced to the minimal amount immediately depending on the severity of hypercalcemia. Do not give to patients on dialysis because hyperphosphatemia may precipitate calcification. Do not give to patients who are at risk for soft-tissue calcification. An estimate of daily calcium intake should be made initially and the intake adjusted as needed. Serum phosphorus should also be determined periodically.

Information for the Patient: Instruct the patient about: 1) compliance with use; 2) adherence to diet instructions and use of vitamin supplement; and 3) symptoms of hypercalcemia. Drug Interactions: PhosLo may decrease the bioavailability of strontium, strontias, strontias, or strontias. Use of PhosLo may lead to metabolic acidosis, hyperkalemia, hypercalcemia, hyperparathyroidism, hypertension, hypercalcemia, hypercalcemia, and hypocalcemia. PhosLo may increase the risk of soft-tissue calcification. PhosLo may interact with other medications, including other calcium supplements.

PHARMACOLOGY: The mechanism of PhosLo in reducing serum phosphorus levels has not been determined. Use to treat hypercalcemia alone or in combination with other medications may be effective. The drug should be continued indefinitely. Use of PhosLo is not recommended for patients with severe, symptomatic hypercalcemia. In patients with severe, symptomatic hypercalcemia, the long-term effects of PhosLo on the progression of renal disease or soft-tissue calcification have not been determined. In patients with severe, symptomatic hypercalcemia, PhosLo should be used with caution.

OVERDOSAGE: Administration of PhosLo in excess of appropriate daily dosage can cause severe hypercalcemia. See ADVERSE REACTIONS.

For medical information on PhosLo, please contact Fresenius Medical Care at 888-321-1418 or visit phoslomed.com
The role of Nck proteins in the development and maintenance of the kidney's podocytes was among the topics that Tony Pawson, MD, highlighted in his state-of-the-art lecture, "Signal Transduction Mechanisms in the Kidney.

A distinguished investigator at the Samuel Lunenfeld Research Institute at Mount Sinai Hospital in Toronto and professor in the department of molecular genetics at the University of Toronto, Pawson told the audience that his research addresses the following questions: how are complex biological structures formed, and how is signal transduction organized in space and time?

Among his laboratory's achievements is the discovery that nephrin-dependent actin reorganization is mediated by the Nck (non-catalytic region of tyrosine kinase adaptor protein) family of Src homology 2 (SH2)/SH3 cytoskeletal adaptor proteins. Nephrin is located at the glomerular slit membrane and is essential to renal function.

Using an inducible transgenic strategy to delete Nck expression in adult mouse podocytes, Pawson's lab found that the loss of Nck protein expression rapidly led to proteinuria, glomerulosclerosis, and altered morphology of foot processes. Podocyte injury also reduced phosphorylation of nephrin in adult kidneys.

Nck likely acts in conjunction with other slit diaphragm proteins to sculpt the architecture of podocytes, Pawson said. He added that Nck is so important to maintaining podocyte morphology that its absence leads to a "corruption of the foot processes" of podocytes. In addition to suggesting that Nck is required to maintain adult podocytes, Pawson's research demonstrated that phosphotyrosine-based interactions with nephrin may occur in foot processes of resting, mature podocytes.

The podocytes of mice were also a focus of a state-of-the-art lecture by Karl Tryggvason, MD, PhD. Mice in which the gene Rhpn1 has been knocked out develop proteinuria and focal segmental glomerulosclerosis.

"This is a novel podocyte-associated gene," he said, referring to Rhpn1 and adding that his lab is now studying the gene and its expression in human disease.

Tryggvason, a professor of medical chemistry at the Karolinska Institute in Stockholm and a member of the Nobel Assembly for physiology or medicine, isolated the defective gene in congenital nephrotic syndrome, leading to the discovery of the novel protein, nephrin.

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A More Paradoxical “Obesity Paradox”: Skinny Dialysis Patients at Increased Risk for Death

The "obesity paradox" became more paradoxical as a result of a poster presentation at ASN Renal Week, with results indicating that hemodialysis (HD) patients with very low body fat are at increased risk of death—even when compared to HD patients with the highest levels of body fat.

Previous large-scale epidemiological studies have documented that a high body mass index is incrementally associated with better survival in patients with chronic kidney disease (CKD) undergoing maintenance hemodialysis.

"The higher the body fat, the greater the survival," Kamyar Kalantar-Zadeh, PhD, of the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, said about the study of 671 dialysis patients at eight California dialysis centers.

"Our study indicates that body fat may be protective in dialysis patients," he said. "The results add to the increasing number of reports about the 'obesity paradox' or 'reverse epidemiology' in patients with CKD and other chronic diseases."

After measuring the patients’ body fat by using near-infrared interactance technology, Kalantar-Zadeh and colleagues divided the patients into five a priori selected body fat percentage groups. A total of 89 patients had a body fat of at least 40 percent.  A body fat of 30 to 39 percent characterized 210 patients. The 10 to 19 percent body fat group included 156 patients. A total of 34 patients had a body fat of less than 10 percent.

The scientists subsequently monitored the mortality rate among the 671 patients over a five-year period (2001–2005). The death rate was 2.5 to 3 times higher among the 34 patients with less than 10 percent body fat than in the most numerous group of patients (210) whose body fat percentage was 20 to 29.

The increased risk of death for patients with very low body fat remained after adjustments for age, sex, race, other illnesses, and key laboratory results for albumin, hemoglobin, phosphorus, total iron binding capacity, ferritin, calcium, and creatinine.

Additional analyses using continuous values of body fat (rather than categories) confirmed a direct, linear relationship between body fat and mortality risk.

The patients were 53.6 ±15.0 years old. Most (52 percent) were men, 30 percent were African American, and 54 percent were diabetic. The mean body fat percentage for the entire group was 27.0 ± 10.5 percent, study co-author Debbie Benner, MS, RD, said at the ASN press briefing about the study.

Nephrologist T. Alp Ikizler, MD, who was moderator of the briefing and was not involved in the study, noted that the results suggest that physicians should be cautious about prescribing weight loss to dialysis patients and emphasize to their patients the health importance of consuming high-quality food. Ikizler is the Catherine McLaughlin Hakim chair in Medicine at Vanderbilt University School of Medicine.

Although more research is needed, the results suggest that the obesity paradox may be explained by an increased risk of death for patients with very low body fat, compared to those with an average—or even very high—body fat.

Like other epidemiological studies, the investigation presented at ASN had observational findings only. "In addition, we estimated body fat by measuring the subcutaneous fat of the upper arm, which may be different from the intra-abdominal fat," Kalantar-Zadeh pointed out.

A National Institutes of Health grant funded the study, whose authors also included Youngmee Kim; Claudia Luna; Amanda Luna; Allen Nissen- son, MD; Debbie Benner; and Csaba Kovesdy, MD.

The study was titled "Association of Body Fat and Survival in Hemodialysis Patients."
U.S. Sees Jump in Survival for Patients on Peritoneal Dialysis

The past few years have witnessed “substantial improvements” in survival among American patients on peritoneal dialysis (PD) relative to those on hemodialysis, according to new research.

That’s a shift from the results of previous U.S. studies, which have tended to show better survival with hemodialysis. “This is a significant contribution to the ongoing debate over hemodialysis versus peritoneal dialysis,” said Peter Blake, MD, of the University of London, Ontario, Canada.

“It is a little unexpected in that it shows PD doing relatively better than in previous U.S. studies,” Blake said. “It brings U.S. findings more into line with those in Canada and Europe.”

Led by Austin G. Stack, MD, MSc, a consultant nephrologist and epidemiologist at the Regional Kidney Centre, Letterkenny General Hospital, Ireland, the researchers analyzed trends in mortality for U.S. hemodialysis and peritoneal dialysis patients across three consecutive time periods: 1995–98, 1999–2001, and 2002–04. The analysis included national data on more than 1 million patients who started dialysis between 1995 and 2004, with follow-up to 2006.

In 2002-04, the risk of death for patients on peritoneal dialysis was significantly lower than for hemodialysis patients, the researchers found.

“In fact, peritoneal dialysis patients experienced a 29 percent lower risk of death at ages under 50 and 18 percent lower at age 50 to 70, compared with patients assigned to hemodialysis,” said Stack. “There was no difference in mortality between peritoneal dialysis and hemodialysis for patients over 70 years.”

Overall mortality for peritoneal dialysis patients decreased by a significant 21 percent from the period 1995-98 to 2002-04, adjusting for differences in case mix. Mortality among hemodialysis patients decreased by only 5 percent between the two calendar periods.

“This is very good news for people who support the use of peritoneal dialysis, in the sense that it’s not only less costly but it’s equally effective…and perhaps more cost-effective when it’s used in the right patient,” Blake added.

So why would the survival rate for those on peritoneal dialysis have changed so much in a 10-year period? “It could involve the development of better practices and newer products and solutions,” Blake said. “Another factor could be the use of cyclers machines at nighttime, which has become widespread. It’s also possible that, as the use of peritoneal dialysis has fallen in the United States, the patient population is a little bit more selected than it was before.”

Of course, he said, the researchers adjusted their analysis for case mix factors.

Stack cited other likely contributing factors, including reduction in peritonitis episodes, better volume control, the emergence of non-glucose containing solutions, and better pre-dialysis care. “The next challenge will be to tease out which of these, if not all, contributed to these improvements in peritoneal dialysis survival.”


Travel Is Linked to Increased Complications in Dialysis Patients

For kidney disease patients on dialysis, international travel can contribute to serious health complications. The findings from the study, “Holiday Travel in Hemodialysis Patients Is Associated with Increased Infection, Loss of Vascular Access, and Anemia,” were presented at Renal Week.

Claire Edwards and Neill Duncan of the Imperial College Kidney and Transplant Institute in London led a team of nurses and other clinicians that prospectively collected health information on patients from satellite units at their medical center who traveled at some point between April 2008 and March 2009. They studied 69 patients, aged 63.6 ± 12.9 years, of diverse ethnic background who traveled on vacation to Europe, the Middle East, India, the United States, Africa, the Pacific Rim, and South Asia.

The researchers noted that during travel, one patient died, and two damaged or lost their fistulas or grafts, (one had revision of his arteriovenous fistula while away, necessitating a temporary central venous catheter, and one required ligation of an infected ulcerated arteriovenous fistula upon return.) A total of 14 units of blood were transfused within one week of return in seven patients, and several patients acquired bloodstream infections. There was a significant decrease in mean hemoglobin from 12.3 ± 0.9 to 11.9 ± 1.0 g/dL (p < 0.05).

These findings indicate that travel is associated with significantly increased infection rates, loss of vascular access, and anemia in dialysis patients.

Edwards said, “We have now measured the risk of travel for our patients, allowing us to give them good counsel,” said Edwards. “This study empowers patients with information in order for them to make choices about their lifestyle.”

The study was presented as part of a session on Dialysis: Epidemiology, Outcomes, and Clinical Trials: Non-Cardiovascular.

Sickle Cell Trait Is More Common in African Americans on Dialysis

The prevalence of sickle cell trait is higher—perhaps twice as high—in African Americans on dialysis, compared to the general African American population, suggests a new study from North Carolina.

Although confirmation is needed, “the high prevalence of sickle cell trait and hemoglobin C trait in the African American ESRD population raises questions about both the potential contribution to renal disease and the effect on the course of patients once they reach ESRD,” said lead researcher Vimal K. Derebail, MD, of the University of North Carolina, Chapel Hill.

Derebail and colleagues analyzed the results of hemoglobin phenotyping in African American adults with end stage renal disease (ESRD) from four dialysis units. The rate of hemoglobinopathies was compared with that in African Americans in the general population, based on newborn screening data from three North Carolina counties in which the four dialysis units were located.

In 188 ESRD patients with available data, the prevalence of sickle cell trait was 14.9 percent—roughly double the 7.1 percent rate in the newborn screening population. The adult dialysis patients also had a higher rate of hemoglobin C trait: 4.8 versus 1.9 percent.

Sickle cell trait has been linked to several different abnormalities of the kidney, and thus might be expected to be more common among African Americans with ESRD. The new results suggest that this is indeed the case—sickle cell trait is found in one in seven of a sample of African American dialysis patients.

Although the findings are preliminary, Derebail said he believes the high rate of hemoglobinopathies could have important implications for African Americans with ESRD. “These less stable hemoglobin could contribute to resistance to treatment of anemia, which is more common in African Americans,” he said. “Additionally, sickle cell trait may be a risk factor for venous thrombosis and as such could affect the longevity of arteriovenous fistulas and grafts used for hemodialysis.

“If sickle cell trait is truly associated with these problems, identification of trait carriers could alter patient management and perhaps change treatment protocols for anemia and more intense monitoring for vascular access thrombosis.”

The results are worthy of confirmation, said Graham Serjeant, MD, chairman of the Sickle Cell Trust in Jamaica. “Presumably many of these patients may have had renal biopsies during the course of their renal investigation. It would be of interest to know whether there was a specific pathology in AS [heterozygous] individuals with ESRD,” he said.

“The well-recognized renal changes in sickle cell trait affect predominantly the medulla and tubular function. There is currently no evidence of an increase in glomerular involvement, which would be the expected mechanism usually accounting for ESRD in patients with homozygous sickle cell (SS) diseases.”

“The significant increase in the prevalence of the hemoglobin C trait—for which there is currently no evidence of tubular or other renal damage—sounds a note of caution in that some aspect of patient selection may have favored subjects with increased frequencies of both AS and AC genotypes,” Serjeant said.

The study, “High Prevalence of Sickle Cell Trait in African-Americans with End-Stage Renal Disease,” was part of the session on “CKD: Disparities in Risk, Access, and Outcomes.”
Key clinical challenges post-renal transplant

Data suggest that although considerable progress has been achieved in outcomes, such as acute rejection rates, these improvements are disproportionate to the gradual improvements made in posttransplant outcomes, such as graft and patient survival (Figure 1).1,3

Figure 1. Adjusted renal allograft and patient survival for deceased non-ECD donor type.*2

<table>
<thead>
<tr>
<th>Year</th>
<th>Graft Survival (n=6523)</th>
<th>Patient Survival (n=5583)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>88.8% (± 0.4%)</td>
<td>95.9% (± 0.2%)</td>
</tr>
<tr>
<td>5 year</td>
<td>93.5% (± 0.2%)</td>
<td>94.5% (± 0.5%)</td>
</tr>
<tr>
<td>10 year</td>
<td>94.6% (± 0.6%)</td>
<td>95.6% (± 0.6%)</td>
</tr>
</tbody>
</table>

*Data from OPTN/SRTTR 2007 Annual Report.
*Patients may have had more than 1 renal transplant.
*Transplant year=1996.
*Non-ECD donor type includes SCDs and DCDs.
*Numbers expressed as percent (standard error).

Multiple factors may compromise posttransplant outcomes4

Chronic renal allograft dysfunction leading to graft failure and death with a functioning graft have been identified as the predominant causes of graft loss after 1-year posttransplant (Figure 2).1

Figure 2. Causes of late allograft loss.1

![Causes of late allograft loss](image)

El-Zoghby et al conducted a longitudinal cohort analysis of 1317 renal transplants performed between January 1996 and July 2006 to identify the causes of renal allograft failure. A mean follow-up of 50.3±32.6 months revealed 25% of grafts were lost (n=330). Of these, 41.8% (n=138) were due to death with function, 11.8% (n=39) due to permanent absence of renal function starting immediately after transplant, and 46.3% (n=153) due to other causes. Some of these other causes include glomerular disease (37%; n=96), fibrosis/atrophy (31%; n=47), medical/surgical conditions (16%; n=25), and acute rejection (12%; n=18).4

CAN: The leading cause of renal allograft failure1

There are multiple causes of chronic allograft nephropathy (CAN) occurring after 1-year posttransplant, including both immunologic and nonimmunologic risk factors. Immunologic factors can include episodes of acute rejection, histocompatibility differences, and suboptimal immunosuppression. Some nonimmunologic factors include donor age, graft quality, hypertension, and hyperlipidemia.1

Histopathologic findings from kidney allografts with CAN reveal features such as interstitial fibrosis, tubular atrophy, fibrous intimal thickening in the arteries, and variable glomerular lesions.1,5,6 These histologic changes may result in clinical manifestations, such as a progressive and irreversible decline in renal function, as evidenced by increased serum creatinine or a decline in glomerular filtration rate (GFR), low-grade proteinuria, and hypertension.1,6,8

References:
2. The Organ Procurement and Transplant Network. OPTN/SRTTR 2007 Annual Report. Transplant data, as of May 1, 2007 Available at: http://www.ustransplant.org/
CV disease is the leading cause of death with a functioning graft posttransplant

To investigate the role of renal function in determining the risk of CV death, Meier-Kriesche et al retrospectively studied 58,900 adult renal transplant recipients who received a primary renal transplant between 1988 and 1998 and who had graft survival of at least 1 year. Of the 5963 patients who died beyond 1 year posttransplant with a functioning graft, 30.1% (n=1797) died due to CV causes. Additional causes of death with a functioning graft included infectious complications, malignancy-related complications, and other, which were responsible for 11.7% (n=698), 10.1% (n=603), and 48.1% (n=2865) of deaths, respectively.

As seen in Figure 3, the risk of CV death significantly increased with serum creatinine levels ≥1.7 mg/dL at 1 year posttransplant (P<0.001).  

### Posttransplant CV and metabolic risk factors may be associated with poor posttransplant outcomes

**Hypertension**

Opelz et al: Patients with higher systolic blood pressure (>140 mm Hg) at 1 and 3 years resulted in an increased risk of graft failure and death (both P<.001).

Opelz et al retrospectively analyzed data from 24,404 adult, de novo, renal transplant recipients who received deceased donor kidneys to examine the relationship between blood pressure control and graft and patient survival up to 10 years.

**Hyperlipidemia**

Dimény et al: Patients with serum cholesterol ≥8.9 mmol L⁻¹ at 6 months posttransplant (n=37) had poorer renal allograft function (serum creatinine >160 μmol L⁻¹) at 2 years than those with lower cholesterol levels (<6.9 mmol L⁻¹, n=69).

In a follow-up study to their prospective trial, Dimény et al evaluated 151 renal allograft transplant patients from 1 center in Sweden, who received transplants between 1989 and 1991, to further assess the effect of hyperlipidemia on posttransplant outcomes.

**Diabetes mellitus**

Kasiske et al: Patients with posttransplant diabetes mellitus (PTDM) had an increased risk for renal allograft failure (relative risk: 1.63), death (relative risk: 1.87), and death-censored graft failure (relative risk: 1.46) (all P<0.0001).

To evaluate the incidence and clinical impact of PTDM, Kasiske et al conducted a retrospective analysis of 11,659 renal transplant patients who were Medicare recipients and received first renal transplants from 1996 to 2000.

Signaling the future: Focusing on clinical challenges to help improve posttransplant outcomes

Continued management of factors contributing to graft dysfunction leading to failure or death with function is important to improve posttransplant outcomes. Clinical strategies that help slow the progression of CAN and reduce the incidence of CV and metabolic risk factors should be considered.
African Americans Have Higher Morbidity After Donating Kidneys than Whites

Group Discussions about Kidney Transplantation Increase Loved Ones’ Willingness to Donate

Lupus Patients Who Receive Kidney Transplants Rarely Develop Lupus Nephritis

Recent lupus nephritis is uncommon in lupus patients who receive a kidney transplant, but the condition often leads to allograft failure with an increased risk of death after transplantation. That was the finding of a study presented recently at Renal Week.

Studies have provided conflicting results about the incidence and severity of the inflammatory condition lupus nephritis in patients with a history of lupus who have received a kidney transplant. To study the issue, Gabriel Contreras, MD, of the University of Miami, and his colleagues analyzed data from the United Network for Organ Sharing to determine the frequency of lupus nephritis in kidney transplant recipients and the risk this condition has for patients. Their analysis included 6850 patients with a history of lupus who received kidney transplants between 1987 and 2006.

The researchers found that lupus nephritis occurred in 2.44 percent of individuals in the study and that it led to a fourfold increased risk of kidney transplant failure. Also, death occurred in approximately 16 percent of affected transplant recipients.

1. Lupus recurring in the kidney transplant as an event is less important than rejection in determining the absolute risk of kidney transplant failure because rejection is a much more frequent event, occurring in 26 percent of the recipients,” said Contreras.

The investigators discovered that African Americans (odds ratio (OR) = 1.71; 95 percent confidence interval (CI) = 1.25–2.34) and young women (OR = 1.69; 95 percent CI = 1.05–2.75) were at higher risk for developing lupus nephritis in their transplanted kidney, but receiving a kidney transplant before or after starting dialysis did not affect one’s risk. The type of kidney transplant (deceased or living donor) also had no effect on a patient’s risk of developing lupus nephritis.

The study, “Recurrence of Lupus Nephritis Following Kidney Transplantation,” was presented as part of a Renal Week session on Transplantation: Epidemiology, Outcomes, Clinical Trials, and Health Services Research.
Recent MDs are Better at Referring Patients For Preemptive Kidney Transplants than Veteran Doctors

Compared with doctors who have been practicing for many years, recent medical school graduates are more likely to refer kidney disease patients for preemptive kidney transplants, according to a study presented at Renal Week.

To investigate, Ladner and her colleagues analyzed data from all adult patients who received a living donor kidney transplant at their institution between March 2007 and May 2009. A total of 529 transplantations were performed; 274 were preemptive, while 255 were performed after dialysis was initiated.

Referring physicians with less time since graduation may provide better care if they learn more about the benefits of preemptive transplantation, the authors said. The authors report no financial disclosures. Study co-authors include Vadim Lyuksemburg, Raymond Chang, Olivia Ross, Juan Carlos Caicedo, MD, Anton Skaro, MD, PhD, John Friedewald, MD, Michael Abecasis, MD, and Jane Holl, MD, all of Northwestern University.

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Artificially Sweetened Sodas Save Calories but not Kidneys

A "significant, twofold increased odds" for a fast decline of kidney function is linked to drinking two or more servings of artificially sweetened soda each day, according to a study presented at ASN Renal Week. Interestingly, a reduction in kidney function was not detected in members of the study population who consumed sugar-sweetened sodas.

According to the industry journal Beverage Digest, Americans consumed an average of 760 eight-ounce servings of soda in 2008. The findings came from an analysis of health data on over 3000 women participating in the Nurses’ Health Study by Julie Lin, MD, FASN, and Gary Curhan, MD, FASN, of Brigham and Women’s Hospital. The association between intake of artificially sweetened beverages and kidney function persisted even after Lin and Curhan accounted for age, caloric intake, obesity, high blood pressure, diabetes, cigarette smoking, physical activity, and cardiovascular disease.

Other studies have questioned the health effects of soda consumption. In 2007, Boston University scientists found that the risk for developing metabolic syndrome is 44 percent higher in people who daily consume one or more cans of diet soda and sugar-sweetened beverage. These findings came from an analysis of the Framingham Heart Study data on over 6000 people who filled out food questionnaires and were followed for an average of four years to gauge the health impact of their soft drink consumption habits. The study, funded by the National Institutes of Health and the American Diabetes Association, was published in the American Heart Association’s journal Circulation.

In addition, Lin and Curhan noted that an association between sugar-sweetened soda and urinary protein was shown in a previous analysis of the nationally representative NHANES III population. However, information on kidney function change was not available then.

“There are currently limited data on the role of diet in kidney disease,” Lin said. “While more study is needed, our research suggests that higher intake of artificially sweetened soda is associated with greater rate of decline in kidney function.”

Because the participants in the study were older Caucasian women, the findings may not be directly applicable to men or people of other ethnicities, noted the scientists. They presented the paper, titled “Association of Sweetened Beverages with Kidney Function Decline,” during a free communication session.

Sodium and Carotene Affect eGFR

Lower dietary sodium and higher carotene intake may reduce a woman’s estimated glomerular filtration rate (eGFR), according to work by Julie Lin, MD, FASN, and Gary Curhan, MD, FASN, of Brigham and Women’s Hospital.

In their poster presentation, “Associations of Diet with Kidney Function Decline,” the scientists did not report significance associations for other nutrients.

The study examined the influence of individual dietary nutrients on eGFR decline in over 3000 women with well-preserved kidney function at baseline between 1989 and 2000. The study participants were women in the Nurses’ Health Study, including 730 nurses with diabetes.

“In women with well-preserved kidney function, higher dietary sodium intake was associated with greater kidney function decline, which is consistent with experimental animal data that high sodium intake promotes progressive kidney decline,” Lin and Curhan reported. In addition to sodium and carotene, nutrients targeted by the scientists included dietary protein (total, animal, vegetable, low-fat dairy, high-fat dairy, total dairy, and non-dairy); dietary fat (total, saturated, trans, mono-saturated, polyunsaturated, animal and vegetable); cholesterol; dietary fiber (total, soluble, and insoluble); anti-oxidant vitamins (vitamins A, C, and E); vitamin D; folate; fructose; and potassium.

Cumulative average energy-adjusted nutrient intake was derived from the participants’ 1984, 1986, and 1990 answers on the Food Frequency Questionnaires, the most common dietary assessment tool used in large epidemiologic studies of diet and health.

Primary outcome was >30 percent decline in eGFR as estimated by the four-variable MDRD equation.

In the study population, the median age was 67 years, 97 percent were Caucasian, 54 percent had hypertension, 24 percent were diabetic, and median eGFR was 85 mL/min/1.73 m² in 1989. A total of 380 women (11.5 percent of the study population) experienced an eGFR decline of more than 30 percent.

New Renal Week symposium honors Steven C. Hebert, who broke open black box of tubule cells

Steven C. Hebert, MD, the board-certified nephrologist and physician-scientist responsible for “breaking open the black box of tubule cells,” was honored at an ASN symposium featuring four former colleagues, who described recent studies that build upon Hebert’s pioneering research on the thick ascending limb’s function and dysfunction in kidney disease.

Serving as moderators of the inaugural Steven C. Hebert Memorial Symposium were Gerhard H. Giebisch, MD, professor emeritus of cellular and molecular physiology at Yale and Robert S. Hoover, MD, assistant professor of medicine at the University of Chicago. Support for the session was provided by an educational grant from Amgen.

Speakers reported recent insights into the role of the potassium channel ROMK in solute reabsorption. WNKs (without lysine [K]) play a role in blood pressure control, and ROMK (renal outer medullary potassium) transports potassium out of cells.

The speakers were:

• Jürgen B. Schnerrmann, MD, chief of the Kidney Disease Branch at the National Institute of Diabetes and Digestive and Kidney Diseases.
• Gerardo Gamba, MD, PhD, professor of medicine at the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán and Instituto de Investigaciones Biomédicas, National University of Mexico.
• Pablo A. Ortiz, PhD, associate professor at Henry Ford Hospital’s division of hypertension and vascular research in Detroit.
• Tong Wang, MD, professor and director of Integrated Kidney Function Core at Yale.

Stem Cells Could Prevent AKI after Cardiac Surgery in High-Risk Patients

A llogeneic mesenchymal stem cells (MSC) could provide an effective new approach to reducing the rate of postoperative acute kidney injury (AKI) in high-risk patients, preliminary research suggests.

Led by Christof Westenfelder, MD, of the University of Utah, Salt Lake City, the researchers performed a phase I clinical trial with allogeneic MSC for the prevention of AKI in 15 patients undergoing coronary artery bypass grafting, with or without valve surgery. All patients had risk factors for AKI: kidney disease or other chronic disease, age older than 65, or bypass time longer than two hours.

All patients received allogeneic MSC according to the dose-escalation design. This form of stem cell therapy has been shown to preserve kidney function three months after ischemia-reperfusion AKI in rats via paracrine actions. In the new trial, there were no apparent adverse effects of MSC administration.

The treatment reduced patients’ postoperative length of stay and hospital readmission rate by about half, compared to closely matched historical controls. At discharge, all patients treated with MSC had normal kidney function—in contrast, about 20 percent of control patients had AKI. Renal function remained normal through six months’ follow-up in MSC-treated patients.

Kidney function declined progressively in the historical controls. Allogeneic MSC shows promise in improving safety and efficacy in preventing AKI and subsequent declines in renal function among cardiac surgical patients at high risk, the researchers said.

“Acute kidney injury is a common complication with high morbidity and mortality rates for which no specific therapy is currently available,” Westenfelder said. “It is also increasingly recognized as the cause of progressive chronic kidney disease, eventually requiring dialysis therapy or a kidney transplant. New therapies for both the prevention and treatment of AKI are urgently needed.”

Based on their phase I results, Westenfelder’s group is planning a phase II multicenter study of MSC for AKI prevention.

“This would be an innovative approach to the prevention of AKI and has tremendous potential,” said Anupam Agarwal, MD, of the University of Alabama at Birmingham.

The study, “Administration of Allogeneic Mesenchymal Stem Cells in Open Heart Surgery Patients is Safe and Prevents Post-operative AKI and Reduces Length of Stay and Readmission Rates: Results of Phase I Trial,” was part of a Renal Week session on Pathophysiology of Kidney Disease: Acute Kidney Injury.

Role of the potassium channel ROMK in solute reabsorption. WNKs (without lysine [K]) play a role in blood pressure control, and ROMK (renal outer medullary potassium) transports potassium out of cells.

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A new IV iron therapy has emerged...

For the treatment of iron deficiency anemia in adult patients with CKD...
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Feraheme is indicated for the treatment of iron deficiency anemia in adult patients with chronic kidney disease.

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

In clinical studies, serious hypersensitivity reactions were reported in 0.2% (3/1,726) of subjects receiving Feraheme. Other adverse reactions potentially associated with hypersensitivity (e.g., pruritus, rash, urticaria or wheezing) were reported in 3.7% (63/1,726) of subjects. Patients should be observed for signs and symptoms of hypersensitivity for at least 30 minutes following Feraheme injection and the drug should only be administered when personnel and therapies are readily available for the treatment of hypersensitivity reactions.

1.9% (33/1,726) of Feraheme-treated subjects experienced hypotension. Please monitor for signs and symptoms of hypotension following each Feraheme injection. Excessive therapy with parenteral iron can lead to excess storage of iron with the possibility of iatrogenic hemosiderosis. Patients should be regularly monitored for hematologic response during parenteral iron therapy, noting that lab assays may overestimate serum iron and transferrin bound iron values in the 24 hours following administration of Feraheme. As a superparamagnetic iron oxide, Feraheme may transiently affect magnetic resonance diagnostic imaging studies for up to 3 months following the last Feraheme dose. Feraheme will not affect X-ray, CT, PET, SPECT, ultrasound, or nuclear imaging.

In clinical trials, the most commonly occurring adverse reactions in Feraheme treated patients versus oral iron treated patients reported in ≥ 2% of chronic kidney disease patients were diarrhea (4.0% vs. 8.2%), nausea (3.1% vs. 7.5%), dizziness (2.6% vs. 1.8%), hypotension (2.5% vs. 0.4%), constipation (2.1% vs. 5.7%) and peripheral edema (2.0% vs. 3.2%). In clinical trials, adverse reactions leading to treatment discontinuation and occurring in 2 or more Feraheme-treated patients included hypotension, infusion site swelling, increased serum ferritin level, chest pain, diarrhea, dizziness, ecchymosis, pruritus, chronic renal failure, and urticaria.

Reference: 1. Feraheme™ Prescribing Information. Please see reverse for brief summary of full Prescribing Information.
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Drug-drug interaction studies with Feraheme were not conducted. Feraheme may reduce the absorption of concurrently administered and iron preparations.

**USE IN SPECIFIC POPULATIONS**

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Feraheme is contraindicated in pregnancy. In animal studies, Feraheme decreased total fetal weight and fetal malformations at maternally toxic doses of 13-15 times the human dose. Use Feraheme during pregnancy only if the potential benefit justifies the potential risk to the fetus. In clinical studies, adverse reactions leading to treatment discontinuation and occurring in ≥ 2 Feraheme-treated patients included hypotension, infusion site swelling, increased serum ferritin level, chest pain, diarrhea, dizziness, ecchymosis, pruritus, urticaria, nausea, and vomiting. In clinical studies, serious hypersensitivity reactions were reported in 0.2% (3/1,726) of patients randomized to Feraheme. Adverse reactions following the first injection of Feraheme were more frequent than those observed following the second injection. In a pseudo-controlled, cross-over trial, 713 patients with CKD received a single 510 mg dose of Feraheme. Adverse reactions reported by these patients were similar in character and frequency to those observed in other clinical trials.

**DRUG INTERACTIONS**

Drug-drug interaction studies with Feraheme were not conducted. Feraheme may reduce the absorption of concurrently administered and iron preparations.

**USE IN SPECIFIC POPULATIONS**

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lower GFR levels and higher albumin excretion rates are commonly observed in the apparently “healthy” elderly. The prevalence of CKD is as high as 40 percent among people over 70, primarily because of the large number of people with GFR 30–59 mL/min/1.73 m² (CKD stage 3), many of whom do not have elevated ACR. The prognosis of earlier stages of CKD is highly variable, with more people dying of cardiovascular disease (CVD) than kidney failure. Based on similar findings around the world, the International Society of Nephrology and International Federation of Kidney Foundations adopted the message for World Kidney Day in 2008 that “CKD is common, harmful, and treatable.” One of the purposes of the KDIGO conference was to identify absolute and relative risks of complications of CKD, including all-cause mortality, CVD mortality, kidney failure, acute kidney injury, and progressive kidney disease.

**Overdiagnosis of CKD a concern**

The main concern about the current definition and classification was the possibility of overdiagnosis of CKD and overuse of resources in the investigation and management of CKD, with our appropriate modifications for variations in prognosis. Specific issues raised were the appropriateness of the GFR thresholds, albuminuria thresholds, and absence of age modifications—since

Josef Coresh, MD, PhD (U.S.). The KDIGO Controversies Conference was tasked with addressing five questions:

1. What are the key outcomes of CKD?
2. What progress has been made in CKD testing (eGFR and albuminuria)?
3. What are the key factors determining prognosis of CKD (e.g., eGFR, albuminuria)?
4. Should the current CKD classification (based on eGFR) be modified to include additional factors associated with prognosis?
5. Should the current CKD definition be modified?

The planning committee invited representatives of studies to contribute data on outcomes of CKD in clinical or research populations in which eGFR and albuminuria had been determined at baseline. Outcomes considered included all-cause mortality, CVD mortality, kidney failure treated by dialysis or transplantation (end stage renal disease), acute kidney injury, and decline in eGFR (progressive CKD). An analytical committee provided a uniform analysis plan for systematic evaluation of the data for each cohort and performed meta-analyses of results provided by the studies. Altogether, more than 50 cohorts submitted data and participated in the conference. Meta-analyses on 1.5 million study participants on a range of outcomes were performed and reviewed. A databook consisting of 1704 pages of cohort data and 464 pages of results of meta-analyses was distributed to all conference participants.

The conference consisted of plenary sessions during which KDIGO Co-Chairs Bertram Kasiske, MD (U.S.), and Kai-Uwe Eckardt, MD (Germany), members of the Planning Committee, Richard Glassock, MD (U.S.), a noted critic of the current definition and classification, and other experts on CKD outlined the background and objectives of the conference. Following plenary sessions, conference participants broke out into smaller groups for in-depth discussions of data and a proposal for revisions, and then reconvened in a plenary session for expression of viewpoints on a number of subjects, including a non-binding vote on questions prepared by the organizers.

The data reviewed showed a strong, consistent gradation in risk for all outcomes of CKD according to the level of estimated GFR and urine ACR across a wide range of study populations. Interestingly, the gradation was linear for all levels of albumin excretion and nonlinear for GFR. In general, increased risk for CKD was noted below a level of GFR around 60 mL/min/1.73 m² and at urinary ACR at all levels above 10 mg/g (the lowest value examined). The risk for cardiovascular mortality and kidney disease outcomes tended to be elevated at a higher eGFR than all-cause mortality. In addition, risk varied according to the cause of kidney disease and other factors, such as age, CVD risk factors, diabetes, hypertension, smoking, hypercholesterolemia, and history of CVD. A strong consensus reached by those present was that the current classification did not adequately describe the severity of CKD, and that predicting prognosis could be improved by the following modifications to the classification:

1. Emphasize classification by cause, if known, in addition to stage.
2. Add albuminuria stages, in addition to GFR stages (ACR < 30 mg/g, 30–300 mg/g, and >300 mg/g).
3. Subdivide CKD stage 3 into two stages (GFR 30–44 and 45–59 mL/min/1.73 m²).

Consensus also emerged that it would be premature to change the current definition of CKD based on levels of GFR or presence of kidney damage. The following recommendations were also adopted by those present:

1. Make no change to the definition based on GFR (<60 mL/min/1.73 m²), regardless of age or sex.
2. Make no change to the level of albuminuria defined as a marker of kidney damage (urine ACR >30 mg/g).

These recommendations need to be codified by a guidelines development group that would include a broader array of disciplines.

The immense and unique database provided by the meta-analyses described by those present: was truly a historical event that will propel this entire field to a new level. The openness of the debate, the rigor of the questions and answers, and the immensity of the data and its analysis was truly remarkable. While much work remains to be done on refining the classification, diagnosis, and prognosis of CKD, there is no doubt that the end product will have as its origins the findings and discussions that were in evidence at the London meeting.

In summarizing the outcome of the conference, Levey said, “The debate reflects a tension in our field caused by the paradigm shift about the basic perspective on CKD—from kidney failure as a life-threatening illness to earlier stages of kidney disease as the target for prevention, detection, evaluation, and management.”

A report from the conference was presented at the American Society of Nephrology annual meeting in San Diego and will be published in Kidney International.
Better predictors of posttransplant outcomes may be needed\textsuperscript{1-4}

Data demonstrated that although posttransplant outcomes have gradually improved over time, these improvements are disproportionate to the considerable progress achieved in other outcomes, such as acute rejection.\textsuperscript{1-4} These findings suggest that acute rejection may not be considered the most reliable predictor of posttransplant outcomes.\textsuperscript{4}

Alternative short-term surrogate markers, such as renal function, histologic findings, and immunologic markers, are being assessed in an effort to address the need for reliable predictors of posttransplant outcomes in renal transplantation.\textsuperscript{4,5}

Is renal function a better predictor of posttransplant outcomes?

Studies demonstrated that renal function has emerged as a better marker than acute rejection in predicting posttransplant outcomes.\textsuperscript{3,6,7} In addition, research has shown that preservation of renal function is important for graft survival.\textsuperscript{3,6}

In a retrospective study of 105,742 de novo or repeat adult renal transplants from living or deceased donors performed between 1988 and 1998, Hariharan et al examined renal function in the first year posttransplant as a variable in determining renal graft survival. Results demonstrated a statistically significant link between renal function and graft survival: elevations in 1-year serum creatinine and change in serum creatinine from 6 to 12 months increase the relative hazard for graft failure (Figure 1).\textsuperscript{3}

When assessing the impact of posttransplant variables on outcomes, 1-year serum creatinine and change in serum creatinine from 6 to 12 months had a significant effect ($P<.0001$) on graft failure. Acute rejection within 1 year, however, did not reach significance ($P=.8853$).\textsuperscript{3}

To evaluate the impact of renal function on posttransplant graft survival in the absence or presence of acute rejection, Meier-Kriesche et al retrospectively studied 38,426 de novo adult renal transplants performed between 1995 and 2001. This study reported that only those acute rejection episodes that impair renal function negatively affect graft survival. Three- and 6-year graft survival rates were comparable among patients who had an acute rejection episode with renal function returning to baseline and those who had no acute rejection episodes (Figure 2). The data showed that in the presence of acute rejection episodes, renal function is the better predictor of posttransplant outcomes.\textsuperscript{8}

Figure 1. Relative hazard for graft failure according to 1-year creatinine and $\Delta$ creatinine values.\textsuperscript{7}

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Figure 2. Kaplan-Meier graph of overall graft survival by acute rejection/GFR grouping levels.\textsuperscript{8}

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Utilizing GFR to evaluate renal function$^{5,9}$

Glomerular filtration rate (GFR), measured through clearance assays, may be a more accurate method of estimating renal function versus serum creatinine by avoiding the dependence on age, gender, race, and body weight.$^6$

In a retrospective study of 447 renal transplant recipients who received organs from deceased donors between 1980 and 1994, Marcén et al examined whether calculated GFR (using the MDRD equation) at 12 months posttransplant was predictive of 10-year graft and patient survival. As seen in Figure 3, results from this study are consistent with the findings from Hariharan et al, 2002, demonstrating renal function, as measured by cGFR, to be an important marker of posttransplant outcomes.$^9$

Figure 3. 10-year graft and patient survival by cGFR levels at 12 months posttransplant.$^9$

References:
Conflicts of Interest: Managing Bias and Creating Transparency

By Caroline Jennette

The 2009 Renal Week Public Policy Sessions got off to a provocative start with a forum on conflicts of interest in medicine.

Allen Detsky, MD, PhD, an economist and general internist at Mount Sinai Hospital in Toronto, Canada, argued that physicians sitting on clinical practice guideline (CPG) committees may be influenced—both consciously and subconsciously—by relationships they have with pharmaceutical companies.

In a survey of 100 physicians who served on CPG committees, Detsky and his colleagues found that the majority (87 percent) had relationships with pharmaceutical companies, and 17 percent accused their colleagues of having conflicts of interest (1). Detsky recommended mentoring junior faculty to stay free of industry influence as a means to become “bias-free” experts on CPG committees.

The degree to which the pharmaceutical industry has inserted itself into academic and professional societies also concerns Detsky. But in one example, where the carpeted and bright displays of the drug companies stand in stark contrast to the cramped poster area. However, he acknowledged that the relationship between the pharmaceutical companies and professional societies is often one of necessity, as the revenue generated from industry helps keep professional meetings operational and keeps their staff employed.

An article published this year in the Journal of the American Medical Association lays out a new standard for professional medical associations (PMA) and their relationships with the medical industry (2). The recommendations include a ban on pharmaceutical and medical device industry funding except for journal advertising and exhibit hall fees as well as a ban on industry support for research and/or fellowships sponsored by PMA. The American Society of Nephrology has prepared its own policy on managing conflicts of interest that also addresses funding industry influence and ensuring that educational activities stay free of industry bias and control (3).

Bernard Lo, MD, continued the conversation on conflicts of interest with the Christopher R. Blagg Endowed Lectureship. Lo, director of the University of San Francisco Program in Medical Ethics, also chaired the Institute of Medicine’s (IOM) Committee on Conflict of Interest in Medical Research, Education, and Practice.

The IOM Committee defines conflict of interest as “a set of circumstances that creates a risk that professional judgment or actions regarding a primary interest will be unduly influenced by a secondary interest.” An example is the subconscious effect that bias can have on practitioners that create the intended and often negative consequences, Lo said. Although the importance of collaboration between academia and industry could be increased at the front end to develop new compounds and other remedies, collaborations at the back end with industry-sponsored clinical trials can create multiple conflicts of interest.

Lo discussed a sampling of recommendations from the IOM Committee on Conflicts of Interest report, published in April 2009 (4). Committee recommendations include:

- Creating a standardized, universal disclosure to decrease the variability between institutions and make the disclosure process easier and less time consuming;
- Establishing a consensus development process to develop continuing medical education that is free of industry influence;
- Creating clinical practice guidelines with no direct funding (general fund acceptable) and with full transparency of guideline members; and
- Requiring governing bodies of institutions engaged in medical research, medical education, patient care, or practice guideline development to establish their own standing committees on institutional conflicts of interest.

Lo noted that health care reform initiatives in both the Senate and the House carry provisions similar to the Physician Payment Sunshine Act 2009 (House Bill 5138/Senate Bill 301), which was introduced earlier this year. These provisions require the makers of drugs, medical devices, and medical supplies to report all payments made to physicians above a certain threshold to a publicly accessible website and highlight the political and public interest in exposing possible conflicts of interest.

Rounding out the Thursday session was Dr. Robert Califf, a cardiologist who heads up the Duke Translational Medicine Institute. Califf made the case that there can be substantial biases in the reporting of clinical trials, but with the current trend toward transparency, people are motivated by the circumstances in which they find themselves. “Bias is part of human nature and is here to stay,” Califf said. He emphasized the importance of acknowledging that bias and including it with open discussion when presenting clinical trial results. Bias can play a detrimental role in all stages of the clinical trial process, from choosing the research question to choosing the design to answer that question, to who has access to the data and who is doing the manuscript review.

References


3. View online here: http://www.asn-online.org/cou.


5. For more information on the clinical trial reporting guidelines, visit: http://publicinfo.clinicaltrials.gov/fdaaa.html.


Health Care Delivery: Lessons from Cleveland, Kaiser, and Canada

A renal week public policy symposium used current health care models to illustrate how care delivery systems can be used to provide more cohesive care to consumers.

Randall Cebul, MD, general internist and director of the Case Western Reserve University Center for Health Care Research and Policy, described the current health care system in most of the nation as fragmented, with physicians having limited accountability and health care consumers frequently changing doctors and health care plans due to unemployment and lack of insurance portability. This fragmentation of care creates what Cebul terms “insurance churn,” a system where insurance companies have little incentive to invest in preventive care and chronic disease management due to the transitory nature of insurance coverage.

The Better Health of Greater Cleveland program was presented as an example of a collaborative care model that works to avoid fragmentation of care by creating a system where health care institutions are accountable through public reporting of clinical outcomes stratified by disease condition, type of insurance, and provider type. The Cleveland program started in 2007, and outcome data have been mixed thus far in terms of results, but this system of open reporting and accountability is expected to increase good health outcomes for patients with chronic diseases. Along with this collaborative care model, Cebul provided several other remedies to fragmentation, including increasing pay for performance incentives, using the patient-centered medical home model, and capitalization of payments to providers.

The opposite of fragmentation of care, according to Alain Enthoven, PhD, a health economist with Kaiser Permanente, is the integrated care model, for which Kaiser is a prime example. The goal of an integrated care model, for which Kaiser is a prime example, is to craft changes to the current system of health care delivery.

Enthoven discussed current health reform efforts to include a public option, stating that integrated delivery systems like Kaiser may be pushed out of the insurance market. He recommended instead that insurance companies need the freedom to compete on their own merit by increasing quality and decreasing costs of care (6).

Aderea Levin, MD, described how “necessity drives innovation” in a fixed system and explained chronic kidney disease and end stage renal disease care through the lens of Canada’s single payer system. The Canadian government distributes funds to 10 provinces that create their own budgets and may add supplemental funding. Citizens with end-stage renal disease or ESRD can receive medical care and never see a bill. Although there is variability among provinces, the universal tenet of nephrology care is “equal care across all stages of the kidney disease continuum, regardless of age or employment.”

The British Columbia Renal Agency, directed by Levin, who is herself a practicing nephrologist, created a “kidney care service delivery framework” that has become a model of care delivery for several other provinces. Health care is delivered within an integrated system combining clinical care based on best practice models, fiscal accountability, and a systemwide information management system. Allied health professionals provide multidisciplinary care for early stage chronic kidney disease (CKD) management, with nephrology care added on as patients get closer to end stage renal disease. Preliminary data from Levin’s cohort have been overwhelmingly positive: Patients seen longer in the early stages of CKD have increased survival once they start on dialysis, patients with an eGFR of <15 maintained kidney function for a median of 18 months before needing dialysis, and despite growing elderly CKD population, dialysis incidence in British Columbia decreased from 5 percent to 3 percent, saving $3.2 million to be used elsewhere in the system.

While the collaborative care, integrated care, and single payer models all have their weaknesses, using successful elements and learning from their mistakes can help policymakers as they continue to craft changes to the current system of health care delivery.

Policy Update

Califf ended his talk with a discussion of new regulations created by the Food and Drug Administration Amendments Act of 2007 (PL110-85, Sec. 85). As of December 2007, all clinical trials were mandated to submit clinical trial data and results to the national ClinicalTrials.gov registry (5). As of September 2009, study investigators must also submit all adverse events to the registry or pay a fine of up to $10,000 a day. The Sunshine Act of 2009 (House Bill 110-85) may help take some of the bias out of data reporting, but Califf urges academia to work on the relationship it has with industry and to get over the “we are good, they are bad” mentality.
Antibiotics Yield Modest Decrease in Recurrent UTIs in Children

For children with risk factors for recurrent urinary tract infections (UTIs), long-term antibiotics prophylaxis has a small but significant preventive benefit, concludes a randomized trial in The New England Journal of Medicine.

The Australian multicenter trial included 576 children with at least one symptomatic UTI. The median age was 14 months; about two-thirds of patients were girls. Vesicoureteral reflux was present in 42 percent, grade III or higher in more than half of cases. Rates of microbiologically confirmed UTIs were compared for children assigned to prophylactic antibiotics (trimethoprim 2 mg/dL plus sulfamethoxazole 10 mg/kg) versus placebo.

Over 12 months, 13 percent of children in the antibiotic group had recurrent UTIs, compared to 19 percent of the placebo group. The number needed to treat to prevent one UTI was 14. The reduction in absolute risk was about the same—six to eight percentage points—across subgroups defined by age, sex, reflux status, or number of previous UTIs.

Large numbers of children receive long-term antibiotics with the goal of preventing recurrent UTIs and resultant kidney damage. However, in the absence of randomized trial data, this practice has been questioned.

The new results show a modest effect of trimethoprim-sulfamethoxazole in reducing the risk of symptomatic UTIs in predisposed children. The benefit appears greatest in the first six months; children whose index infection is resistant to trimethoprim-sulfamethoxazole may not benefit.


Erythropoietins Linked to Increased Mortality in Kidney Transplant Patients

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Serum Amyloid P: A New Inhibitor of Renal Fibrosis?

Serum amyloid P (SAP)—a known inhibitor of pulmonary and cardiac fibrosis—may also have antifibrotic effects in the kidneys, according to a study published in Science Translational Medicine.

In experiments in two models of renal fibrosis in mice, administration of human SAP (hSAP) was associated with dose-dependent reductions in fibrosis. Although fibroblasts were still present in similar numbers, hSAP treatment was associated with down-regulation of fibrotic collagen gene transcription and collagen protein deposition. Further experiments suggested that hSAP selectively localized to the injured kidneys, mainly associated with apoptotic and necrotic cells. In humans, more severe kidney disease was associated with lower plasma concentrations of hSAP.

In the kidneys, fibrosis depends on inflammatory monocytes and macrophages, rather than fibroblasts. The antifibrotic effect of hSAP appeared to occur via monocyte/macrophage binding and suppression, dependent on interleukin-19 and regulated binding to Fcy receptors.

There is an urgent need for new treatments directed against chronic inflammation with fibrosis. A natural soluble pattern recognition receptor, SAP has been shown to recognize danger-associated molecular patterns (DAMPs) on the membranes of apoptotic cells and promote Fcy receptor-dependent phagocytosis.

Ray Harris

What are the responsibilities of the ASN Program Committee and how many times a year does it meet?

There are three meetings during the course of the year. The first meeting is held immediately after the ASN annual meeting has concluded, the second is held in mid-January, and the third is held in mid-July.

The initial meeting lasts one afternoon, and the other two meetings are held over the weekend.

The program committee is chosen to reflect the diversity of research and clinical interests of the ASN membership. Each program committee member develops themes and speakers for symposia and oversees the abstract categories in his or her area of expertise. This latter activity includes choosing the abstract reviewers and working with the chairs of the abstract review sessions to develop oral and poster sessions.

How is the ASN Program Committee different from the ASN Postgraduate Education Committee in terms of responsibilities and objectives?

In general, it is the goal of the Program Committee to develop symposia and invite speakers to highlight the latest advances in all areas of nephrology. The symposia developed by the Postgraduate Education Committee are designed to be educational and to update attendees on generally accepted state-of-the-art practices for subject areas.

What were the main highlights from this year’s ASN annual meeting?

This year’s program covered major areas in basic, translational, and clinical sciences. The four featured topics were: Epithelial Transport and Cell Biology, Renal Immunology and Transplantation, New Insights into Glomerular Structure and Function, and Kidney Development and Stem Cells.

Each topic was the focus of a Meeting-Within-a-Meeting (MWM) consisting of oral and basic science symposia as well as free communication sessions. To encourage scientific interchange and to make the annual meeting more user-friendly, each MWM was held in the same area throughout the week. ASN encourages abstract submissions that present new research findings in areas covered by the featured topics.

What was new at this year’s meeting?

We were extremely pleased to present a Steven C. Hebert Memorial Symposium in honor of the late Dr. Hebert’s many scientific achievements.

In addition, a session on late-breaking clinical trials featured the results of a number of large trials, including the FAVORIT trial, the TREAT trial, and the ROADMAP trial.

How do you decide which programs go into Renal WeekEnds?

These decisions are made by the chair for Renal WeekEnds, in association with the ASN Education Committee.

What are the typical challenges you and the committee members encountered in planning for Renal Week?

Do you think one year of preparation is enough to execute a program?

The biggest challenge of the program committee is obtaining commitments from speakers to participate. Luckily, this year’s program committee consisted of individuals who were very organized, diligent, and persistent, so we were able to attract a stellar group of speakers.

What is your advice to your successor and to next year’s committee members?

David Ellison will be the chair of next year’s Program Committee, and I know that he has already chosen another outstanding group of committee members. Just as I did, David served as a committee member for two years prior to becoming chair, so he is well versed in the operations of the committee, and I am absolutely certain that the 2010 ASN meeting will be wonderful.

I would like to be a member of the ASN Program Committee and be involved in preparation for Renal Week. What would you advise me to do?

The program committee is chosen to represent the diversity of the research and clinical activities of ASN members. Therefore, a committee member should have an area of expertise in order to effectively develop symposia and oversee the abstracts.

The committee members are usually chosen three to six months before the next year’s ASN annual meeting. Although no guarantee of success, an individual may contact the program chair for upcoming meetings to volunteer as a potential committee member.
Amgen Lawsuit Alleges Kickback Scheme to Spur Sales of Aranesp

The same day that a major national lawsuit was announced against it, Amgen released the published results from TREAT (the Trial to Reduce Cardiovascular Events with Aranesp Therapy), a large, randomized, double-blind, placebo-controlled, Phase III study of patients with chronic kidney disease. Published in the New England Journal of Medicine and presented at the ASN annual meeting, the study showed the anemia drug Aranesp failed to meet its primary objectives of a reduction in all-cause mortality and found a higher risk of stroke for patients on Aranesp compared with those taking a placebo.

The lawsuit was not about the performance of the anemia drug, however, but about the performance of the drug company representatives, who allegedly encouraged medical providers to bill insurers for samples of Aranesp that were supposed to be free to patients.

The suit alleges a subtle process through which Amgen, based in Thousand Oaks, Calif., provided beyond the usual amount of overfill in Aranesp samples while using less overfill in Procrit samples. Procrit is also manufactured by Amgen, but it is sold by Amgen’s competitor, Johnson & Johnson.

The suit says that Amgen told medical practices that they would make more money if they used Aranesp, because they could bill insurers for that extra amount—whether they gave it all to a single patient or saved the extra portions to give to other patients, according to a report in The New York Times. The lawsuit also alleges that Amgen invited doctors on retreats and paid them for food and lodging, as well as for payment as advisers.

David Polk, a spokesperson for Amgen, said that the company could not comment on the lawsuit, but that Amgen has a solid compliance program and a code of conduct that employees are encouraged to follow.

The suit, filed in federal court in Massachusetts, includes plaintiffs in New York, California, Delaware, the District of Columbia, Florida, Hawaii, Illinois, Indiana, Louisiana, Massachusetts, Michigan, Nevada, New Hampshire, Tennessee, and Virginia.

Toward a Wearable Kidney


The idea that a two-pound, comfortable AWAK (Automated Wearable Artificial Kidney) could be coming is heartening news for patients, and the company spoke of two pounds as a goal. Right now, the AWAK is a six-pound battery-operated prototype. The kidney would provide continuous dialysis through a peritoneal dialysis platform.

AWAK Technologies hopes to begin clinical trials soon, perhaps in early 2010, in Singapore and Los Angeles. The AWAK Technologies website notes that the company hopes the product will be commercially licensed by 2011.

The device works by infusing dialysate into the peritoneal cavity so dialysis can occur. “What differentiates AWAK from either existing peritoneal dialysis or hemodialysis technology is that it is both wearable and self-contained,” the company states. “Patients are able to live their lives with unrestricted mobility. More importantly, they do not have to regularly replace the dialysate as the AWAK continually regenerates the used dialysate through a sorbent cartridge.”

The technology is based on original joint research done at the University of California, Los Angeles, and the U.S. Department of Veterans Affairs.

In 2007, Xcorporeal of Los Angeles completed a study of its artificial kidney prototype and demonstrated feasibility. However, Xcorporeal was delisted from the NYSE AMEX exchange in August 2009 because the company had large financial losses.

Alexion’s Soliris Approved for Orphan Drug Status

Two international bodies approved the drug Soliris (eculizumab) for orphan drug status, giving manufacturer Alexion Pharmaceuticals, Inc., of Cheshire, Conn., special consideration on its way through the drug approval process. Orphan drugs are those that most likely wouldn’t be developed because of the rarity of the disease they treat, in this case atypical hemolytic uremic syndrome (aHUS).

The prognosis for aHUS patients is grim. About 70 percent of patients with the most common mutation for aHUS experience chronic renal insufficiency, chronic dialysis, or death within one year of the first clinical episode.

Both the U.S. Food and Drug Administration and the European Commission have approved the orphan status. The intervention by government on behalf of orphan drug development can take a variety of forms, including tax incentives, better patent protection, and financially subsidized clinical research.

Alexion is currently enrolling patients in four clinical studies of Soliris as an investigational treatment for adolescent and adult patients with aHUS. Clinical studies are also currently being planned on the use of Soliris as a treatment for children with aHUS.

If the drug is approved for treatment, the drug’s orphan status would let Alexion market Soliris for 10 years exclusively in Europe and for seven years exclusively in the United States.

NxStage Announces FREEDOM Study Interim Results

NxStage Medical announced results from its FREEDOM (Following Rehabilitation, Economics and Everyday-Dialysis Outcome Measurements) trial during Renal Week 2009.

The FREEDOM study is a multicenter prospective cohort study designed to measure the clinical and economic benefits of daily home hemodialysis compared with conventional, thrice-weekly, in-center hemodialysis. Key interim findings included:

- a nearly 50 percent reduction in the average number of prescribed antihypertensive medications over 12 months;
- discontinuation of antihypertensive medications by 33 percent of patients; and
- a 50 percent or greater decrease in use of antihypertensive medications among 56 percent of patients.

Additional FREEDOM data demonstrated a 40 percent reduction in expected mortality of patients using daily home hemodialysis therapy with the NxStage System One compared with patients from the United States Renal Data System.

Letters

ASN Kidney News accepts letters to the editor in response to published articles. Please submit all correspondence to kidneynews@asn-online.org
Triage® NGAL Test
For Fast Quantitative Determination of NGAL*
in about 15 minutes
in EDTA whole blood or plasma