cyte depletion in rats expressing human diphtheria toxin receptor transgene. *J Am Soc Nephrol* 16: 2941–2952, 2005
8. Lasagni L, Romagnani P: Glomerular epithelial stem cells: The good, the bad, and the ugly. *J Am Soc Nephrol* 21: 1612–1619, 2010
9. Appel D, Kershaw DB, Smeets B, Yuan G, Fuss A, Frye B, Elger M, Kriz W, Floege J, Moeller MJ: Recruitment of podocytes from glomerular parietal epithelial cells. *J Am Soc Nephrol* 20: 333–343, 2009
10. Matsusaka T, Sandgren E, Shintani A, Kon V, Pastan I, Fogo A, Ichikawa I: Podocyte injury damages other podocytes. *J Am Soc Nephrol* 22: 1275–1285, 2011
11. Mollet G, Ratelade J, Boyer O, Muda AO, Morisset L, Lavin TA, Kitzis D, Dallman MJ, Bugeon L, Hubner N, Gubler MC, Antignac C, Esquivel EL: Podocin inactivation in mature kidneys causes focal segmental glomerulosclerosis and nephrotic syndrome. *J Am Soc Nephrol* 20: 2181–2189, 2009
12. Sato Y, Wharram BL, Lee SK, Wickman L, Goyal M, Venkatareddy M, Chang JW, Wiggins JE, Lienczewski C, Kretzler M, Wiggins RC: Urine podocyte mRNAs mark progression of renal disease. *J Am Soc Nephrol* 20: 1041–1052, 2009
13. Ichikawa I, Ma J, Motojima M, Matsusaka T: Podocyte damage damages podocytes: Autonomous vicious cycle that drives local spread of glomerular sclerosis. *Curr Opin Nephrol Hypertens* 14: 205–210, 2005
14. LeHir M, Kriz W: New insights into structural patterns encountered in glomerulosclerosis. *Curr Opin Nephrol Hypertens* 16: 184–191, 2007
15. Abbate M, Zoja C, Morigi M, Rottoli D, Angioletti S, Tomasoni S, Zanchi C, Longaretti L, Donadelli R, Remuzzi G: Transforming growth factor-beta1 is up-regulated by podocytes in response to excess intraglomerular passage of proteins: A central pathway in progressive glomerulosclerosis. *Am J Pathol* 161: 2179–2193, 2002
16. Benzing T: Signaling at the slit diaphragm. *J Am Soc Nephrol* 15: 1382–1391, 2004
17. Dreier JP: The role of spreading depression, spreading depolarization and spreading ischemia in neurological disease. *Nat Med* 17: 439–447, 2011
18. Peti-Peterdi J, Sipos A: A high-powered view of the filtration barrier. *J Am Soc Nephrol* 21: 1835–1841, 2010
19. Giardino L, Armelloni S, Corbelli A, Mattinzoli D, Zennaro C, Guerrot D, Tourrel F, Ikehata M, Li M, Berra S, Carraro M, Messa P, Rastaldi MP: Podocyte glutamatergic signaling contributes to the function of the glomerular filtration barrier. *J Am Soc Nephrol* 20: 1929–1940, 2009
20. Brenner BM, Meyer TW, Hostetter TH: Dietary protein intake and the progressive nature of kidney disease: The role of hemodynamically mediated glomerular injury in the pathogenesis of progressive glomerular sclerosis in aging, renal ablation, and intrinsic renal disease. *N Engl J Med* 307: 652–659, 1982
21. Schonenberger E, Ehrich JH, Haller H, Schiffer M: The podocyte as a direct target of immunosuppressive agents. *Nephrol Dial Transplant* 26: 18–24, 2011

See related article, "Podocyte Injury Damages Other Podocytes," on pages 1275–1285.

Declining Renal Function in Persons of Different Race without Chronic Kidney Disease

Robert N. Foley and Allan J. Collins
University of Minnesota School of Medicine, Minneapolis, Minnesota

J Am Soc Nephrol 22: 1183–1184, 2011.
doi: 10.1681/ASN.2011050521

"Plus ça change, plus c'est la même chose"—the more things change, the more they stay the same. Although this epigram is generally attributed to a 19th-century man of letters from France,[1] it could easily have been coined by nephrologists in the United States with an interest in racial disparities in the burden of ESRD. Thus, two articles reporting outcomes seen in the initial years of ESRD coverage by Medicare note that hypertension and diabetes are the two most common causes, incidence rates are almost 3 times higher in African Americans, and survival was longer in African Americans than in Caucasians.

This ESRD paradox of higher incidence rates and longer survival remains unresolved to this day. Surprisingly, the recent explosion of research into quantifying the burden and risk factors of chronic kidney disease (CKD) has failed, so far, to cut the Gordian knot. Despite greater burdens of modifiable risk factors such as obesity, hypertension, and diabetes, creatinine-based GFR ($GFR_{creatinine}$) values are typically higher among minority populations. Of note, abnormal albuminuria is also overrepresented. This scenario of higher GFR and abnormal albuminuria finds an obvious parallel in classic type 1 diabetic nephropathy. Sadly, this parallel does not seem to apply: Racial disparities are not mitigated—if anything, they widen when levels of albuminuria are accounted for.

Most recent CKD models assume that loss of GFR proceeds in an orderly, linear fashion. In this model, GFR levels in two populations could reach a single (low) GFR level in different ways as follows: one subgroup starts at a higher GFR but loses GFR more quickly; the other starts at a lower level but loses GFR more slowly. All things being equal, if this model of different lines converging on a single point is valid, two things should follow: GFR levels are never the same in the two populations until the point of convergence is reached, and the disparity should be narrower at lower GFR levels. In this regard, it is instructive that the National Health and Nutrition Examination Survey III dataset shows the odds of having GFR <60 and <30 ml/min per 1.73 m^2 with the Modification of Diet in Renal Disease equation are 0.57 and 0.54, respectively, when African Americans were compared with Caucasians. In other words, the disparity, if anything, widened as GFR levels fell.

As the paradoxes have accumulated, so has concern that reliance on $GFR_{creatinine}$ estimating equations may underlie these disparate findings.[4] Hence, the findings of Peralta and colleagues in this issue of *JASN* are highly germane.[5] Using the community-based Multi-Ethnic Study of Atherosclerosis da-

Published online ahead of print. Publication date available at www.jasn.org.

Correspondence: Dr. Allan J. Collins, University of Minnesota School of Medicine, 914 South Eighth Street, Suite S-406, Minneapolis, MN 55404. Phone: 612-347-5811; Fax: 612-347-5980; E-mail: acollins@usrds.org

tabase, GFR levels were measured longitudinally using creatinine- and cystatin-C-based methods. If cystatin-C is truly a more accurate marker of GFR than serum creatinine,[6] then this design is very attractive because it should give a truer measure of GFR trajectories.

The Peralta *et al.* study had all of the inherently attractive features of all prospective studies that incorporate regularly scheduled assessments of analytes such as kidney function. This being said, some of the design features demand reflection. Despite careful follow-up, the available follow-up time is comparatively small, and the average number of GFR assessments per study subject is modest at approximately 2.8. The study excluded 11% of subjects because creatinine-based estimated GFR ($eGFR_{creatinine}$) was <60 ml/min per 1.73 m^2, and GFR trajectories in the excluded population might be very informative. A unique feature of this study was the diversity of race and ethnicity in the study population. On a cautionary note, GFR estimating equations probably need to be validated in each separate ethnic group. Death also has potential to be a competing event, and comparative death rates were not reported in the study. If, as seems plausible, GFR loss was accelerating between the last available GFR test and death, GFR declines might be underestimated in the subgroup with the highest mortality rate. Incident cases are classically defined with a denominator consisting of the population without the condition of interest. Because subjects with a cystatin-C-based estimated GFR ($eGFR_{cystatin\ C}$) < 60 at baseline were not formally excluded, the proportion of subjects with $eGFR_{creatinine} \geq 60$ and $eGFR_{cystatin\ C} < 60$ may not have been trivial. In addition, the modest numbers of incident cases available probably prevent definitive quantification of racial disparities at this point.

Regarding cystatin-C-based GFR ($GFR_{cystatin\ C}$), an important finding of this study was a more rapid rate of decline in kidney function in African American participants, a disparity that could not be explained by participant characteristics at study inception. Returning to the previously mentioned hypothesis of linear convergence at ESRD from different starting GFRs, it is noteworthy that baseline $GFR_{cystatin\ C}$ levels are identical in African American and Caucasian subgroups at 94 ml/min per 1.73 m^2. The situation for $eGFR_{creatinine}$ could be described as "the same but different": Although GFR loss patterns appear similar when based on serum creatinine, baseline GFR values are clearly lower in Caucasian participants.

Although this paper provides important insights, it appears that we still have a pattern of observations that amounts to "a riddle wrapped in a mystery inside an enigma, but perhaps there is a key."[7] Regarding racial disparities in CKD and trajectories of GFR, this study suggests that models other than linear convergence should be considered.

DISCLOSURES

None.

REFERENCES

1. Available at: http://en.wiktionary.org/wiki/plus_ça_change, _plus_c'est_la_même_chose. Accessed May 2011.
2. Eggers PW, Connerton R, McMullan M: The Medicare experience with end-stage renal disease: Trends in incidence, prevalence, and survival. *Health Care Financ Rev* 5: 69–88, 1984
3. Krakauer H, Grauman JS, McMullan MR, Creede CC: The recent U.S. experience in the treatment of end-stage renal disease by dialysis and transplantation. *N Engl J Med* 308: 1558–1563, 1983
4. Ibrahim HN, Wang C, Ishani A, Collins AJ, Foley RN: Screening for chronic kidney disease complications in US adults: Racial implications of a single GFR threshold. *Clin J Am Soc Nephrol* 3: 1792–1799, 2008
5. Peralta CA, Katz R, DeBoer I, Ix J, Mark Sarnak M, Kramer H, Siscovick D, Shea S, Moyses Szklo M, Shlipak M: Racial and ethnic differences in kidney function decline among persons without chronic kidney disease. *J Am Soc Nephrol* 22: 1327–1334, 2011
6. Peralta CA, Katz R, Sarnak MJ, Ix J, Fried LF, De Boer I, Palmas W, Siscovick D, Levey AS, Shlipak MG: Cystatin C identifies chronic kidney disease patients at higher risk for complications. *J Am Soc Nephrol* 22: 147–155, 2011
7. Churchill W: BBC broadcast, "The Russian Enigma," London, United Kingdom, October 1, 1939

See related article, "Racial and Ethnic Differences in Kidney Function Decline among Persons without Chronic Kidney Disease," on pages 1327–1334.

Sunrise of Statins after AURORA and 4D?

Christoph Wanner and Vera Krane
Department of Medicine I, Division of Nephrology, University of Würzburg, Würzburg, Germany

J Am Soc Nephrol 22: 1184–1186, 2011.
doi: 10.1681/ASN.2011050504

Ten years ago, a placebo-controlled trial of statin treatment for hemodialysis patients was considered unethical by many nephrologists. In 2005, to the surprise of many, the results of the 4D study (the German Diabetes and Dialysis Study)[1] demonstrated that lowering LDL cholesterol with atorvastatin (20 mg/d) in 1255 hemodialysis patients with type 2 diabetes did not produce statistically significant reductions in the primary outcome measure. Four years later, AURORA (A Study to Evaluate the Use of Rosuvastatin in Subjects on Regular Hemodialysis: An Assessment of Survival and Cardiovascular Events)[2] was hoped to provide clarification of whether LDL

Published online ahead of print. Publication date available at www.jasn.org.

Correspondence: Dr. Christoph Wanner, Department of Medicine, Division of Nephrology, University Hospital, Oberdürrbacher Strasse 6, 97080 Würzburg, Germany. Phone: 49-931-201-39300; Fax: 49-931-201-639300; E-mail: wanner_c@medizin.uni-wuerzburg.de