

fore, it is difficult to determine whether increased concentrations of resistin are the cause or the consequence of inflammation within the vascular wall, oxidative stress, or vascular dysfunction associated with hypertension.

Much needs to be learned about the relationship among adipokines, inflammation, hypertension, and the cardiovascular system. Nevertheless, the study of Zhang *et al.*¹⁵ adds a piece to the emerging evidence that adipokines may contribute to the pathogenesis of chronic conditions. In the future, we should focus much more on the role of adipose tissue. Obesity is a causative factor in the development of hypertension and is linked to inflammation and chronic kidney disease.^{18,19} Among implicated mechanisms such as increased sodium retention, sleep disturbance, activation of the renin-angiotensin system and sympathetic nervous system, and insulin resistance, the release of adipokines may play an adjunctive role in the increased risk for hypertensive diseases. These molecules may provide incremental value in the prediction of cardiovascular risk beyond current schemes and approaches.

DISCLOSURES

None.

REFERENCES

- Wićcek A, Kokot F, Chudek J, Adamczak M: The adipose tissue: A novel endocrine organ of interest to the nephrologist. *Nephrol Dial Transplant* 17: 191–195, 2002
- Steppan CM, Bailey ST, Bhat S, Brown EJ, Banerjee RR, Wright CM, Patel HR, Ahima RS, Lazar MA: The hormone resistin links obesity to diabetes. *Nature* 409: 307–312, 2001
- Koerner A, Kratzsch J, Kiess W: Adipocytokines: Leptin—the classical, resistin—the controversial, adiponectin—the promising, and more to come. *Best Pract Clin Endocrinol Metab* 19: 525–546, 2005
- Patel L, Buckels AC, Kinghorn IJ, Murdock PR, Holbrook JD, Plumpton C, Macphee CH, Smith SA: Resistin is expressed in human macrophages and directly regulated by PPAR γ activators. *Biochem Biophys Res Commun* 300: 427–476, 2003
- Reilly MP, Lehrke M, Wolfe ML, Rohatgi A, Lazar MA, Rader DJ: Resistin is an inflammatory marker of atherosclerosis in humans. *Circulation* 111: 932–939, 2005
- Lehrke M, Reilly MP, Millington SC, Iqbal N, Rader DJ, Lazar MA: An inflammatory cascade leading to hyperresistinemia in humans. *PLoS Med* 1: e45, 2004
- Bokarewa M, Nagaev I, Dahlberg L, Smith U, Tarkowski A: Resistin, an adipokine with potent proinflammatory properties. *J Immunol* 174: 5789–5795, 2005
- Verma S, Li SH, Wang CH, Fedak PW, Li RK, Weisel RD, Mickle DA: Resistin promotes endothelial cell activation: Further evidence of adipokine-endothelial interactions. *Circulation* 108: 736–740, 2003
- Kougias P, Chai H, Lin PH, Yao Q, Lumsden AB, Yao Q, Chen C: Adipocyte-derived cytokine resistin causes endothelial dysfunction of porcine coronary arteries. *J Vasc Surg* 41: 691–698, 2005
- Calabro P, Samudio I, Willerson JT, Yeh ET: Resistin promotes smooth muscle cell proliferation through activation of extracellular signal-regulated kinase 1/2 and phosphatidylinositol 3-kinase pathways. *Circulation* 110: 3335–3340, 2004
- Hung HF, Wang BW, Chang H, Shyu KG: The molecular regulation of resistin expression in cultured vascular smooth muscle cells under hypoxia. *J Hypertens* 26: 2349–2360, 2008
- Frankel DS, Vasan RS, D'Agostino RB, Benjamin EJ, Levy D, Wang TJ, Meigs JB: Resistin, adiponectin, and risk of heart failure: The Framingham Offspring study. *J Am Coll Cardiol* 53: 754–762, 2009
- Takata Y, Osawa H, Kurata M, Kurokawa M, Yamauchi J, Ochi M, Nishida W, Okura T, Higaki J, Makino H: Hyperresistinemia is associated with coexistence of hypertension and type 2 diabetes. *Hypertension* 51: 534–539, 2008
- Papadopoulos DP, Makris TK, Krespi PG, Poulakou M, Stavroulakis G, Hatzizacharias AN, Perrea D, Votteas VV: Adiponectin and resistin plasma levels in healthy individuals with prehypertension. *J Clin Hypertens* 7: 729–733, 2005
- Zhang L, Curhan GC, Forman JP: Plasma resistin levels associate with risk for hypertension among nondiabetic women. *J Am Soc Nephrol* 21: 1185–1191, 2010
- Bo S, Ciccone G, Durazzo M, Gambino R, Massarenti P, Baldi I, Lezo A, Tiozzo E, Pauletto D, Cassader D, Pagano G: Efficacy of antioxidant treatment in reducing resistin serum levels: A randomized study. *PLoS Clin Trials* 2: e17, 2007
- Bo S, Gambino R, Gentile L, Pagano G, Rosato R, Saracco GM, Cassader D, Durazzo M, Cavallo-Perin P: High-normal blood pressure is associated with a cluster of cardiovascular and metabolic risk factors: A population-based study. *J Hypertens* 27: 102–108, 2009
- Ix JH, Sharma K: Mechanisms linking obesity, chronic kidney disease, and fatty liver disease: The roles of fetuin-A, adiponectin, and AMPK. *J Am Soc Nephrol* 21: 406–412, 2010
- Ramos LF, Shintani A, Ikizler TA, Himmelfarb J: Oxidative stress and inflammation are associated with adiposity in moderate to severe CKD. *J Am Soc Nephrol* 19: 593–599, 2008

See related article, "Plasma Resistin Levels Associate with Risk for Hypertension among Nondiabetic Women," on pages 1185–1191.

Neighborhoods, Race, and Nephrology Care

Sharon Stein Merkin

Division of Geriatrics, Geffen School of Medicine, University of California, Los Angeles, Los Angeles, California

J Am Soc Nephrol 21: 1068–1070, 2010.
doi: 10.1681/ASN.2010050534

Access to nephrology care is essential to mitigating the progression of renal failure.¹ There is some evidence of racial disparities with regard to this care, disparities whereby black individuals are less likely to receive timely care compared with their white counterparts.² The underlying causes of these racial differences are not fully understood but most likely include a combination of socioeconomic and social factors. In this issue

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

Correspondence: Dr. Sharon Stein Merkin, Division of Geriatrics, Geffen School of Medicine at UCLA, 10945 Le Conte Avenue, Suite 2339, Los Angeles, CA 90095-1687. Phone: 310-825-8253; Fax: 310-794-2199; E-mail: smerkin@mednet.ucla.edu

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of *JASN*, Prakash *et al.*³ explore the association between living in a predominantly black neighborhood and obtaining nephrology care before the onset of ESRD.

Prakash *et al.*³ list some of the characteristics of predominantly black neighborhoods that might affect health outcomes and behaviors, including lack of availability of healthful foods and recreational facilities as well as cultural and health beliefs. There is strong evidence, however, that this segregation of minorities into distinct neighborhoods also runs along socioeconomic boundaries. Data from the National Health and Nutrition Examination Survey (NHANES), a nationally representative sample of the United States, shows not only that white and black populations are segregated in distinct communities but also that those neighborhoods are distinct in terms of socioeconomic status (SES) to the point that there is little overlap between them.⁴ Thus, even among low socioeconomic neighborhoods, black individuals live in more disadvantaged areas compared with their white counterparts.⁴ The spatial isolation of minorities into disadvantaged neighborhoods may be driving the racial disparities in access to nephrology care.

Although some researchers have considered standard neighborhood socioeconomic factors when evaluating racial disparities in kidney disease,^{5–7} few studies have examined additional neighborhood characteristics beyond SES that might influence kidney disease. As Prakash *et al.*³ suggest, racial composition may also reflect issues related to community support and cultural barriers, factors that may not be adequately captured by traditional socioeconomic indicators. One study examining racial composition and dialysis treatment and outcomes indeed found that living in predominantly black neighborhoods was associated with increased time to transplantation and dialysis facilities with lower quality of care.⁸

Although Prakash *et al.*³ also consider only patients who had already initiated renal replacement therapy, the study focus is on nephrology care pre-ESRD, a factor that could potentially mitigate the progression of renal dysfunction and adverse outcomes after the initiation of dialysis. The issue of nephrology care before ESRD is particularly salient, considering that Medicare is available to all patients with ESRD. This suggests that racial disparities in ESRD morbidity are likely due to distinctions in previous health care access and use that mitigate or exacerbate progression of kidney disease to ESRD. This outcome is thus valuable in that it has the potential to identify a modifiable factor in preventing progression.⁹

Prakash *et al.*³ found the likelihood of nephrology care decreases in areas with increasing proportions of black residents. They also found, however, that once nephrology care was initiated, the quality of care was not associated with racial composition.

A major strength of this study is its use of the US Renal Data System, a comprehensive database that is estimated to include 93% of US adults with a diagnosis of ESRD. The authors acknowledge several limitations of their study, including its use of zip code-level data to define area. One limitation that is not mentioned, however, is that the contextual effects that the authors observed at the zip code level may have been confounded by the

individual-level socioeconomic conditions of its residents. Because this data set does not provide a variety of measures of individual SES (limited to employment status and medical insurance coverage), residual confounding is likely.

Nonetheless, the choice of predictor and outcomes in this particular study by Prakash *et al.*³ contributes to its public health importance and policy implications. By examining racial composition, the authors chose to focus on an element of racial disparities that might be associated with a particular area and its available resources rather than limit the focus to individual-level factors. Considering the important role of public health in implementing interventions at the community level, this focus is crucial for pinpointing the needs and characteristics of community-level interventions.

Similarly, the focus on nephrology care highlights additional public health ramifications with regard to kidney disease and ESRD in particular. Nephrology care represents a preventive measure that might significantly mitigate progression of kidney disease and outcomes. Prakash *et al.* tackle these issues even further by exploring additional quality-of-care outcomes, including later referrals, type of dialysis, and renal transplantation. They did not find an association between racial composition and quality of nephrology care, further emphasizing the significance of focusing on access to nephrology care in high-risk areas as a way to reduce morbidity and mortality related to ESRD.

Future research should expand on these ideas in three ways. First, there is a need to investigate further the link between racially isolated communities, in this case predominantly black, and low nephrology care. Aside from issues that Prakash *et al.*³ suggest in directing future research, including assessing proximity to dialysis facilities and degree of urbanization, other factors have been associated with these racially isolated neighborhoods that might be instrumental in affecting access to nephrology care. These include physical neighborhood features, such as including lack of street connectivity and walkability,^{10,11} as well as social factors, such as social support and trust of the health care system.^{12,13} There is some debate in the literature as to how racial composition operates in terms of influencing health. Although some have found that racially isolated neighborhoods are associated with adverse health outcome among black individuals,¹⁴ others have found racial homogeneity to be beneficial, in particular for Hispanic communities.¹⁵ Moreover, one recent study showed that social capital (a measure of social trust, cooperation, and civic engagement) modified the effects of racial composition, with black neighborhoods with high social capital exhibiting low rates of mortality compared with other neighborhoods.¹⁶ Thus, additional neighborhood factors and populations should be considered in evaluating the associations between racial composition and access to nephrology care.

A second direction for future research is to examine the role of these neighborhood factors in influencing health care access and use and possibly preventing the onset of kidney dysfunction.¹⁷ This association found by Prakash *et al.* with regard to nephrology care indicates that the same barriers to such care are likely to affect

general health care access. This may address racial disparities in incidence of ESRD, as well as risk factors such as hypertension and diabetes that rely on adequate health care management and control to prevent disease progression.¹⁸

Finally, future research should consider other minority populations as well. Recent data show the Hispanic population in the United States experiences higher incidence rates of ESRD and a faster progression from chronic kidney disease to ESRD compared with non-Hispanic white individuals.¹⁹ Most studies on racial disparities, however, do not include Hispanic participants. This signifies a growing need to include the Hispanic population in future studies on racial or ethnic disparities in kidney disease.

DISCLOSURES

None.

REFERENCES

- Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, Hogg RJ, Perrone RD, Lau J, Eknoyan G, National Kidney Foundation: National Kidney Foundation practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. *Ann Intern Med* 139: 137–147, 2003
- Ifudu O, Dawood M, Iofel Y, Valcourt JS, Friedman EA: Delayed referral of black, Hispanic, and older patients with chronic renal failure. *Am J Kidney Dis* 33: 728–733, 1999
- Prakash S, Rodriguez RA, Austin PC, Saskin R, Fernandez A, Moist LM, O'Hare AM: Racial composition of residential areas associates with access to pre-ESRD nephrology care. *J Am Soc Nephrol* 21: 1192–1199, 2010
- Merkin SS, Basurto-Dávila R, Karlamangla A, Bird CE, Lurie N, Escarce J, Seeman T: Neighborhoods and cumulative biological risk profiles by race/ethnicity in a national sample of U.S. adults: NHANES III. *Ann Epidemiol* 19: 194–201, 2009
- Volkova N, McClellan W, Klein M, Flanders D, Kleinbaum D, Soucie JM, Presley R: Neighborhood poverty and racial differences in ESRD incidence. *J Am Soc Nephrol* 19: 356–364, 2008
- Shoham DA, Vupputuri S, Diez Roux AV, Kaufman JS, Coresh J, Kshirsagar AV, Zeng D, Heiss G: Kidney disease in life-course socioeconomic context: The Atherosclerosis Risk in Communities (ARIC) Study. *Am J Kidney Dis* 49: 217–226, 2007
- Merkin SS, Coresh J, Roux AV, Taylor HA, Powe NR: Area socioeconomic status and progressive CKD: The Atherosclerosis Risk in Communities (ARIC) Study. *Am J Kidney Dis* 46: 203–213, 2005
- Rodriguez RA, Sen S, Mehta K, Moody-Ayers S, Bacchetti P, O'Hare AM: Geography matters: Relationships among urban residential segregation, dialysis facilities, and patient outcomes. *Ann Intern Med* 146: 493–501, 2007
- Striker G: Report on a workshop to develop management recommendations for the prevention of progression in chronic renal disease. *J Am Soc Nephrol* 5: 1537–1540, 1995
- Rundle A, Roux AV, Free LM, Miller D, Neckerman KM, Weiss CC: The urban built environment and obesity in New York City: A multilevel analysis. *Am J Health Promot* 21[Suppl]: 326–334, 2007
- Rundle A, Neckerman KM, Freeman L, Lovasi GS, Purciel M, Quinn J, Richards C, Sircar N, Weiss C: Neighborhood food environment and walkability predict obesity in New York City. *Environ Health Perspect* 117: 442–447, 2009
- Armstrong K, Ravenell KL, McMurphy S, Putt M: Racial/ethnic differences in physician distrust in the United States. *Am J Public Health* 97: 1283–1289, 2007
- Piette JD, Heisler M, Krein S, Kerr EA: The role of patient-physician trust in moderating medication nonadherence due to cost pressures. *Arch Intern Med* 165: 1749–1755, 2005
- White K, Borrell LN: Racial/ethnic neighborhood concentration and self-reported health in New York City. *Ethn Dis* 16: 900–908, 2006
- Inagami S, Borrell LN, Wong MD, Fang J, Shapiro MF, Asch SM: Residential segregation and Latino, black and white mortality in New York City. *J Urban Health* 83: 406–420, 2006
- Hutchinson RN, Putt MA, Dean LT, Long JA, Montagnet CA, Armstrong K: Neighborhood racial composition, social capital and black all-cause mortality in Philadelphia. *Soc Sci Med* 68: 1859–1865, 2009
- Mehrotra R, Kermah D, Fried L, Adler S, Norris K: Racial differences in mortality among those with CKD. *J Am Soc Nephrol* 19: 1403–1410, 2008
- Powe NR: Let's get serious about racial and ethnic disparities. *J Am Soc Nephrol* 19: 1271–1275, 2008
- Lora CM, Daviglius ML, Kusek JW, Porter A, Ricardo AC, Go AS, Lash JP: Chronic kidney disease in United States Hispanics: A growing public health problem. *Ethn Dis* 19: 466–472, 2009

See related article, "Racial Composition of Residential Areas Associates with Access to Pre-ESRD Nephrology Care," on pages 1192–1199.

Stem Cell Therapy for the Kidney: A Cautionary Tale

Andras Nagy*[†] and Susan E. Quaggin*^{‡§}

*Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Ontario, Canada; and Departments of [†]Molecular Genetics and [‡]Medicine, and [§]Division of Nephrology, St. Michael's Hospital, University of Toronto, Toronto, Ontario, Canada

J Am Soc Nephrol 21: 1070–1072, 2010.
doi: 10.1681/ASN.2010050559

Over the past few years, tremendous advances have occurred in stem cell biology. With the development of induced pluripotent stem cell technology, it is now possible to reprogram adult cells to differentiate into multiple cell types, including renal cells.¹ Although induced pluripotent stem cells hold great promise for treatment of chronic diseases such as kidney failure in the future, current therapies are limited to readily available endogenous progenitor cell populations that can be isolated or mobilized from the bone marrow. These include hematopoietic stem cells (HSCs), mesenchymal stem cells, and endothelial progenitor cells, collectively known as bone marrow-derived cells (BMDCs).

Therapies to enhance mobilization of endogenous BMDCs or infusions of BMDCs have been used in preclinical models of renal disease that include ischemia-reperfusion injury, the

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

Correspondence: Dr. Susan E. Quaggin, Samuel Lunenfeld Research Institute, TCP Building, Room 5-1015-2, 25 Orde Street, Toronto, Ontario M5T 3H7, Canada. Phone: 416-586-4800; Fax: 416-586-5130; E-mail: quaggin@lunenfeld.ca

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