Kidney International, Vol. 68 (2005), pp. 414–424

NEPHROLOGY FORUM

Ethnicity and renal disease

Principal discussant: JOHN FEEHALLY

Leicester General Hospital, Leicester, United Kingdom

CASE PRESENTATION

A 63-year-old woman of South Asian origin, a Gujerati-speaking Hindu, was admitted 5 years ago to the renal unit at Leicester General Hospital for further evaluation of chronic kidney disease (CKD). She was born in India, moved to East Africa as a child, and migrated from Malawi to the United Kingdom in 1972. Her medical history included four uneventful pregnancies. She has no history of diabetes mellitus or hypertension. Three of her cousins had developed type 2 diabetes in the fourth decade of life, and her deceased aunt developed end-stage renal disease (ESRD) in the seventh decade of life and required renal replacement therapy (RRT).

Three months before admission, the patient had reported increasing tiredness and was found to have a normochromic normocytic anemia, which was unresponsive to oral iron supplementation. On admission she reported continuing tiredness and breathlessness on moderate exertion, with no angina, cough, sputum, or wheeze. She reported nocturia for the previous 5 years but no other urinary symptoms. A review of systems was otherwise unremarkable. She was a vegetarian, a non-smoker, and she drank no alcohol.

On examination she was clinically anemic and overweight [body mass index (BMI), 31 kg/m^2]. Her blood pressure was 145/90 mm Hg, the cardiovascular examination was otherwise normal, and all peripheral pulses were preserved with no bruits. The lung fields were clear. Abdominal examination revealed no masses, and the pelvic examination was normal. She had a waddling gait. Laboratory investigations revealed hemoglobin, 8.9 g/dL; mean corpuscular volume, 90 fl; white blood cell count, 4.3 $\times$ 109/L with normal differential; ferritin, 53 μg/L; C-reactive protein (CRP), <5 mg/L; plasma sodium, 135 mmol/L; potassium, 5.0 mmol/L; urea, 21 mmol/L [blood urea nitrogen (BUN), 59 mg/dL); serum creatinine, 345 mol/L (3.9 mg/dL); estimated glomerular filtration rate (GFR), 19 mL/min; serum bicarbonate, 15 mmol/L; albumin, 35 g/L; total protein, 74 g/L; serum calcium, 1.9 mmol/L; phosphate, 1.9 mmol/L; alkaline phosphatase, 326 IU/L; serum 25-OH vitamin D_3, 6 IU/L; and intact parathyroid hormone (iPTH), 42 pmol/L. Autoantibody screen and serologic tests for lupus were normal. An ultrasound scan showed symmetrical shrunken kidneys (7 cm bipolar length) with smooth outlines and no evidence of stones or hydronephrosis. Urinalysis disclosed 1+ protein, no blood, and a bland urine sediment with only occasional hyaline casts. The urine albumin-to-creatinine ratio was 15 mg/mmol.

Initial treatment included oral sodium bicarbonate supplementation. Blood pressure was controlled at 130/80 mm Hg with atenolol and amlodipine. Hemoglobin was corrected to 11.5 g/dL with intravenous iron and subcutaneous erythropoietin. Serum calcium and phosphate were controlled with dietary modification, calcium carbonate, and alfacalcidol. Her renal function steadily deteriorated, and 3 months after initial evaluation she was established on continuous ambulatory peritoneal dialysis (CAPD). Within 6 months, technique failure was associated with recurrent peritonitis. She was established on regular hemodialysis (HD) with a right internal jugular PermCath followed by three unsuccessful attempts to establish an arteriovenous fistula sufficient for regular dialysis. One year after dialysis was initiated, she received a living-related renal transplant from her

The Nephrology Forum is funded in part by grants from Amgen, Incorporated; Merck & Co., Incorporated; and Dialysis Clinic, Incorporated.

Key words: chronic kidney disease, end-stage renal disease, hypertension, diabetes mellitus.

son. Transplantation was unremarkable and the graft functioned immediately. Three years later, she is well with excellent graft function [serum creatinine, 88 mol/L (1.0 mg/dL)] and she takes prednisolone and tacrolimus for maintenance immunosuppression.

DISCUSSION

PROFESSIR JOHN FEEHALLY (*The John Walls Renal Unit, Leicester General Hospital, Leicester, United Kingdom*): People from indigenous or migrant ethnic minority populations have increased susceptibility to CKD, and the woman whose case is discussed here is in many ways typical. She first presented to the renal service with advanced CKD of undeterminable cause and a family history of CKD and type 2 diabetes, although the patient herself is not diabetic. She was already anemic and acidotic, had metabolic bone disease, and soon required RRT. After periods on peritoneal dialysis (PD) and HD with considerable technical challenges, she received a successful kidney transplant from a living-related donor.

As well as the challenges of understanding and reversing the epidemic of CKD exemplified by this woman, there are major public health implications in delivering the increased demands for RRT in areas serving minority populations. In this Nephrology Forum, I shall review our current knowledge of the epidemiology of CKD in ethnic minority populations, the likely pathogenetic mechanisms underlying the epidemic, the interventions likely to detect and reduce the epidemic, as well as the public health implications of the increased demand for RRT. I shall focus in particular on emerging evidence in the United Kingdom but shall also maintain an international perspective.

Epidemiology

The migration of ethnic minority populations to the United Kingdom has occurred rapidly in the last half-century and continues to accelerate. A sharp increase in the African Caribbean population in the United Kingdom started in the 1950s; then a rapid migration of South Asians occurred in the early 1970s from sub-Saharan Africa when political change created insecurity for a large South Asian population originally migrant from the Indian subcontinent. Recently a more diffuse migration has gained momentum, particularly from a number of other African populations. The ethnic minority population in the United Kingdom continues to grow and now comprises 8% of the general population. For example, in the 1991 census, South Asians were 8.4% of the Leicestershire population, but 22% of those living within the city boundary of Leicester. By the time of the 2001 census, more than 50% of those living within the Leicester city boundary were of South Asian origin (the term South Asian applies to people originating from the Indian subcontinent and includes people from a wide range of cultural and religious heritages, including Hindus, Sikhs, and Muslims, and the term Asian describes people originating from China, Japan, and other countries on the western Pacific Rim). All such migrations bring with them challenges to health care. Even if migrant populations had no variations in disease susceptibility, substantial language and cultural variations would provide additional demands on the health care system. In fact, disease variations in the United Kingdom's South Asian population include marked increases in susceptibility to type 2 diabetes, coronary heart disease, and CKD [1, 2]. African Caribbeans have an additional susceptibility to severe hypertension and the subsequent end organ damage. The South Asian population in the United Kingdom also has a younger age distribution than the indigenous white population, so that diseases such as CKD, which increase in incidence with increasing age, will at first be underrepresented compared to the eventual population burden as the minority population ages.

Worldwide epidemiologic evidence indicates that the incidence of CKD is increased in many ethnic minority populations. Most studies have used the onset of ESRD and acceptance for RRT as a means of case ascertainment, but this approach might underestimate the true incidence if patients have inequity of access to RRT. There a is three- to fourfold increase in the incidence of ESRD in South Asian and African Caribbean populations in the United Kingdom [2, 3], and there are similar increases in African Americans, Hispanics, and Native Americans in the United States [4, 5]. Other populations at increased risk include Aborigines, Maoris, and Pacific Islanders in Australasia.

It is common for us to emphasize the increased susceptibility to ESRD in these ethnic minority populations. But perhaps we should instead consider that the white European population is uniquely at low risk of renal disease. This decreased risk could be due to genetic reasons, or because in most white populations, the environmental changes of urbanization were imposed so much more slowly.

In more homogeneous populations, the incidence of ESRD is even more strikingly increased. Members of the Native American Pima tribe have a specific susceptibility to diabetic nephropathy [6], whereas Native Americans of the Zuni Pueblo tribe, with an incidence of ESRD 18 times that of white Americans, have a broader susceptibility to CKD as well as diabetic nephropathy and glomerulonephritis [7]. The Aboriginal population in Tiwi Island, Northern Territory, where obesity and type 2 diabetes are endemic, has an ESRD incidence more than 2000/million population/year; comprising only 26% of the population of Northern Territory, Aborigines are 96% of those on RRT [8].

All these ethnic minority populations at increased risk of CKD share a marked increase in susceptibility to type 2 diabetes, with an increased susceptibility among diabetics to ESRD. For example, data from Leicester indicated a 13-fold increase in the risk of a South Asian diabetic developing ESRD compared to a white diabetic [9], the Pima Indians have a risk of ESRD 14 times that of the white United States population [10], and there is also a marked increase in African American type 2 diabetics compared to whites. Current predictions suggest an increase in the prevalence of type 2 diabetes of 30% to 50% above current levels by the year 2025 in developed countries, but two- to threefold increases in prevalence in developing countries during the same period [11]. This predicted epidemic of ESRD in people with diabetes will be uncontainable unless effective preventive strategies are developed.

As well as susceptibility to diabetic ESRD, the other major cause of ESRD in the black population is hypertension. Other causes of ESRD have been less well studied, but data from Leicester and Hammersmith Hospital also indicate increases in the incidence of glomerulonephritis as well as reflux nephropathy in South Asians [2]. Furthermore there is an excess of patients in whom the cause of renal disease is not identified; they typically present with advanced renal impairment, bland urine findings, and shrunken kidneys on renal imaging and thus do not undergo renal biopsy [2]. A more recent study confirms the wide range of renal pathology that is increased in the South Asian population and suggests that a substantial proportion of those cases of undetermined cause constitute chronic tubulointerstitial nephritis (TIN). The causes of the TIN have not been elucidated [12]. Corticosteroid therapy has been used with some benefit, although this approach has not been rigorously studied. Sporadic evidence suggests that tuberculosis is sometimes an etiologic agent; centers treating such South Asian populations typically identify a small number of such patients whose renal function improves in response to antituberculous treatment [13].

Studies using requirement for RRT for case ascertainment will not distinguish susceptibility to the development of renal disease from an increased risk of progression to ESRD once nephropathy is established. In hypertensive blacks, there is long-established evidence of increased progression risk despite equivalent blood pressure control [14]. In CKD of other etiologies, evidence increasingly points to the increased risk of progression as the predominant explanation for increased ESRD. A United States birth cohort analysis showed no difference between blacks and whites in the prevalence of CKD, yet 5 years later in the same cohort, a near fivefold increased risk of ESRD among the blacks was apparent [15]. Recent screening data from London also show no difference in the prevalence of early CKD between white and South Asian populations despite the marked excess of ESRD in South Asians [Lightstone L, unpublished observations].

The Australian Aborigines in Tiwi Island have the unenviable reputation of being among the least healthy people in the world. The high incidence of ESRD as well as endemic obesity and type 2 diabetes are associated with a standardized mortality ratio more than four times that of whites living in the same area and a sixfold increase in cardiovascular deaths [16]. This is a potent reminder that ESRD carries with it more risks than merely the consequences of lifelong RRT. Accelerated cardiovascular disease is the major cause of death in all ESRD populations. In all populations that have been studied, proteinuria, even if it has not resulted in renal failure, is an independent risk factor for such cardiovascular mortality.

Pathogenesis

Genetic susceptibility to renal diseases and their progression, susceptibility provoked by environmental factors, susceptibility induced by the effects of fetal environment, and socioeconomic influences all can contribute to susceptibility to CKD in ethnic minority populations [17–19]. Substantial indirect evidence supports a genetic basis for susceptibility. This evidence includes the increased risk of renal disease among the first-degree relatives of ethnic minority populations with ESRD [20], even when the confounding variable of consanguinity is taken into account. The marked increase in susceptibility to diabetic nephropathy in the Pima Indians suggests a genetic influence in that population. Genetic evaluation of the Zuni Indians might prove more informative, because their broader susceptibility to CKD has more similarity to the South Asian population. That is, they carry a double jeopardy not only of susceptibility to type 2 diabetes but also an independent susceptibility to CKD. The African Caribbean population likewise has susceptibility to type 2 diabetes, but their renal disease risk is made more complex by the additional susceptibility to end-organ damage from hypertension [21] and sickle cell disease.

While new approaches to analysis of the human genome hold out much promise, no genes linked with susceptibility to CKD have been identified in ethnic minority populations. Even in a population with as much apparent homogeneity as the Pima Indians, a genome-wide search strategy has identified possible susceptibility loci on four different chromosomal regions [22]. A number of substantial collections of DNA from probands in ethnic minority populations with ESRD are being established around the world to facilitate genetic studies, for example, a multi-ethnic cohort of 10,000 probands with diabetic ESRD in the United States [23]. Even though epidemiologic data suggest a broad increase in susceptibility to ESRD in South Asians, the enormous cultural, religious, and social variety among South Asians must be

recognized. One study in Pakistan indicates that one's ethnic subgroup influences the prevalence of proteinuria [24]. Cohorts assembled for DNA studies therefore must be of sufficient size and mix to minimize the risk that any ethnic stratification confounds study findings.

Many racial groups have an increased susceptibility to renal disease, and this issue has particularly been explored in the context of type 2 diabetes, as populations undergo rapid urbanization. One favored hypothesis has been that these populations exhibit a "thrifty genotype," [25] which has become dominant through natural selection, as it confers the capacity to lay down fat and carbohydrate stores in response to occasional plenty among prolonged periods of famine, and was therefore an ideal genotype for survival among hunter-gatherers. When confronted with sustained plenty, such a genotype, unless environmentally rigorously controlled, creates susceptibility to the "metabolic syndrome" (obesity, insulin resistance, type 2 diabetes, and dyslipidemia), vascular disease, and with it an increased risk of renal disease. Another view favors the existence of a "thrifty phenotype" in which intra-uterine and early life environments create an acquired metabolic state adapted for relative starvation but with increased susceptibility to the metabolic syndrome. However, when social and environmental circumstances allow increased access to food in childhood and adult life, "catch-up" weight gain ensues, again resulting in the metabolic syndrome [26, 27]. Identifying the relative contributions of genetic and environmental influences is hampered by the relative paucity of population-based studies for establishing the true incidence of renal disease in the regions where these migrant populations originate.

The hypothesis of Barker et al [28] emphasizes the impact of the fetal environment on subsequent adult disease, proposing that in utero "programming" contributes to adult disease. The basis of the hypothesis is epidemiologic evidence in the United Kingdom and elsewhere that low birth weight, due to intra-uterine growth retardation rather than to prematurity, is associated with increased adult risk of type 2 diabetes, insulin resistance, coronary heart disease, and hypertension, although the association with hypertension has recently been challenged [29]. Starvation at puberty might similarly predispose to cardiovascular disease [27]. It is of course difficult to distinguish between in utero effects and those of subsequent adverse environmental factors that in early life might be closely associated with the same circumstances that provoke maternal undernutrition. It is additionally proposed that low birth weight reduces nephron number and increases susceptibility to systemic hypertension and renal disease [30], and there is evidence in whites of a relationship between primary hypertension and nephron number [31]. Considerable indirect evidence also suggests that in utero programming contributes to adult renal disease. The kidney is particularly susceptible to fetal malnutrition because 60% of nephrons are formed in the third trimester; evidence also indicates that kidney size is disproportionately reduced in babies who are small for gestational age [32], although there are no data in this study on ethnicity. Recent autopsy studies also confirm an association among low birth weight, reduced nephron number, and increased glomerular size, a factor known in a variety of experimental studies to increase the risk of glomerulosclerosis [33, 34]. Evidence exists of increased glomerular size in African Americans and Pima Indians, but autopsy studies did not confirm any additional impact of ethnicity modifying the relationship between glomerular characteristics and birth weight. Thus, it is low birth weight per se that likely carries the increased susceptibility. In the Tiwi Island Aborigine population in whom 25% have a birth weight less than 2500 g, a direct association exists between low birth weight and increasing risk of adult proteinuria, and systolic blood pressure and proteinuria are inversely related to kidney length and volume [35].

Finally, powerful evidence indicates that socioeconomic disadvantage is associated with increased risk of ESRD [18, 36], a complex interaction that might directly influence renal damage, be associated with damaging health behaviors, or influence the quality of health care of those with kidney disease.

Effective interventions

The Barker hypothesis suggests that reductions in infant mortality since the 1960s in many parts of the world will result in the survival to adult life of large cohorts of low-birth-weight infants at risk of renal and other chronic diseases. This phenomenon should abate if birth weights continue to increase.

General population screening for hypertension and diabetes, followed by their effective early management, are well established strategies that will reduce both cardiovascular risk and the risk of CKD. Screening for CKD has never been advocated in the United Kingdom; although the costs and implications of progressive CKD are substantial, its relative rarity has never been considered as justifying population-wide screening. Although only moderate systematic evidence supports screening, the International Society of Nephrology recently advocated screening of high-risk populations in developed countries, including ethnic minority populations (*www.isn-online.org*). Which screening tools are most appropriate remains under investigation. The prime justification for screening is that earlier intervention can delay or prevent the onset of renal failure. It is proposed that nearly one-half of the excess ESRD risk in African Americans can be explained on the basis of potentially modifiable risk factors [37]. Powerful evidence suggests that tight

blood pressure control is a highly effective strategy for slowing progression of CKD, and when proteinuria is present, therapy should comprise blockade of the renin-angiotensin system (RAS) by angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) or perhaps by an ACE inhibitor and ARB in combination. Little evidence suggests that unique strategies are required to minimize the progression of CKD in ethnic minority populations [38]. No known unique risk factors suggest that information from clinical trials should be applied differently in these populations. Studies showing benefits of renin-angiotensin blockade in diabetic and non-diabetic proteinuric nephropathy have been undertaken predominantly in whites, but the African American Study of Kidney Disease and Hypertension (AASK) study clearly shows the benefits of including an ACE inhibitor in the treatment regimen when proteinuria exceeds as little as 300 mg/24 hours [39]. Poor control of risk factors for CKD is universal, and the challenge is developing approaches that ensure a wide application of lifestyle changes, equitable access to health care that is culturally specific, and best clinical practice in all population settings.

Encouraging evidence from the very high risk Australian Aboriginal population in Tiwi Island suggests that these goals can be achieved. A community-based study identified high-risk patients (blood pressure > 140/90 mm Hg, diabetes with microalbuminuria, or overt proteinuria without diabetes). Although not a randomized control trial, a community education intervention was introduced that emphasized strategies for reducing obesity and improving diabetic control with ACE inhibitor treatment. The outcome of this intervention was striking: within 3 years there was measurable benefit in improved blood pressure control, significant reduction in proteinuria, and reductions in the incidence of ESRD and overall mortality [40]. Regrettably, the same investigators now report evidence of regression of this benefit when funding for the initiative was not maintained; this outcome demonstrates the need for a sustained public health commitment if real and sustained health gains are to be made (Hoy W, unpublished observations).

In the United States, considerable evidence points to blacks having inferior access to health care. Blacks report receiving less information about health care and express more dissatisfaction with treatment [41]. Fewer black hypertensive patients have their blood pressure checked at least annually. These differences are reported at all income levels, although blood pressure control might be more unsatisfactory among blacks living in inner cities [42]. The only similar study in the United Kingdom shows a more reassuring trend for earlier referral of blacks with CKD compared to whites. [43].

Early detection and intervention for preventing or delaying CKD are the long-term health goals, but it is also important that RRT be delivered with equity in ethnic minority populations. In the United States, mortality in patients receiving RRT (adjusted for socioeconomic factors and comorbidity), is consistently lower in ethnic minorities [4]. One single-center study in the United Kingdom showed no difference in mortality [44], but the United Kingdom Renal Registry reports a significant reduction in one-year mortality for blacks on RRT, although no difference between South Asians and whites (Byrne C et al, unpublished data). In Hong Kong, survival of Chinese patients undergoing PD is significantly better than that reported in other large PD studies involving predominantly white populations [45]. The reasons for these discrepant outcomes are not clear and require further study. Ethnicity itself might not be the explanation, and many other factors might introduce bias. For example, 80% of all dialysis patients in Hong Kong are undergoing PD compared to the predominance of HD in the United States. A low patient acceptance also might alter the case mix; only 54% of Hong Kong Chinese identified as suitable for PD agreed to receive the treatment [46]. A low transplantation rate, as in Hong Kong, also might lead to younger, fitter patients remaining on PD, thus improving the cohort outcome.

Data from Leicester show that ethnicity does not influence the risk that complications from dialysis will necessitate that patients change to another treatment modality. Nor does ethnicity affect problems related to vascular access or hospital admission rates (Carr S, unpublished observations). However, in Leicester, in the 1980s non-English–speaking South Asians established on CAPD were more likely to switch to HD because of the consequences of peritonitis (Carr S, unpublished observations). It is reassuring that a range of improvements in dialysis-related care, including increased language and culture-specific resources, eliminated that inequality in subsequent time periods, and data from another United Kingdom South Asian population confirms no difference in infection rate or technique survival [44]. In a black urban PD population in the United States, no difference in PD peritonitis was detected [47].

Registry data from several parts of the world, including the United Kingdom and the United States, are consistent in showing inequity of access to renal transplantation or at least a lower rate of transplantation. Ethnic minority populations are overrepresented in dialysis programs but less likely to be listed for cadaveric transplantation, wait longer, and are less likely to receive allografts (Rudge CJ et al, unpublished observations). Ethnic minority populations are under-represented among cadaveric donors so are more likely to receive poorly matched kidneys. Graft survival, however, is not inferior in South Asians in the United Kingdom [48], although it is significantly worse in blacks in the United States [49]. The most disadvantaged

of all are patients who do not receive a cadaveric kidney or a kidney from a live donor.

Promotion of live donor transplantation is a key element in strategies for minimizing inequity of access to transplantation. A study from Baltimore showed that a decade of active encouragement of volunteerism led to the same live donor transplant rate in blacks as whites, with equivalent patient and graft survival, and median waiting times below the national average [50]. Innovative approaches to live donor transplantation, for example, strategies aimed at transplanting across ABO incompatibility barriers, also might assume special importance. United States physicians asked why ethnic minority patients were referred less frequently for transplantation most commonly cited the lack of a potential live donor, patient preference, comorbidity, or concern that patients did not complete necessary evaluations [51].

In South Asian populations, the high prevalence of blood group B compared to a majority white donor population with blood group O is a significant limiting factor in cadaveric transplantation. Haji et al [52] recently proposed that kidneys from A2 donors might be suitable for B recipients if anti-A antibody titers are low, which appears to be the case in blood group B South Asians on the transplant waiting list, unless there is positive panel reactivity indicating previous sensitization. However, this strategy has not yet been prospectively tested. Human leukocyte antigen (HLA) matching algorithms for allocation of cadaveric kidneys disadvantage ethnic minority populations. A retrospective analysis has investigated the impact of removing HLA-B matching as a priority for cadaveric kidney allocation, so that in the absence of a 000 mismatch, the kidney should be allocated on the basis of DR matching alone. The analysis suggests that this approach would increase non-white transplants by 6%, reduce white transplants by 4%, and increase graft loss by 2% [53].

The shortage of cadaveric donors from ethnic minority populations is a continuing concern. In the United Kingdom, South Asians and blacks only contribute 1.5% of the total donor pool yet comprise 6% of the general population and 19% of patients on the cadaveric transplant waiting list (Rudge CJ, unpublished observations). The reasons underlying this shortfall have been extensively explored with these communities, and programs are in place to improve donor rates through awareness and education, although progress is slow.

Tools for the evaluation of health-related quality of life are now available for renal disease and have been extensively evaluated. However, these are almost exclusively written in English, have been developed and tested in white populations, and might not be sensitive to the cultural, religious, and social distinctions in ethnic minority populations. Important differences also might emerge when questionnaire-based quality-of-life assessment relies on the use of health professionals, interpreters, and family members. These potential biases will not be infrequent, even in stable migrant populations, in which older people do not read or write in English or even in their native language.

Nevertheless, South Asians in the United Kingdom reported inferior quality of life compared to whites both on PD and HD, and following renal transplantation [54]. However, health-related quality of life in the Dialysis Outcomes and Practice Patterns Study (DOPPS) was higher in ethnic minority patients [55]. The prominence of religious belief as a coping mechanism has been suggested as a possible explanation for this finding [56]; alternatively, in the United States health care setting, a narrowing of the gap in access to good quality health care after the initiation of RRT might alter perception of quality of life. There have been no substantial evaluations of quality of life in ethnic groups in pre-dialysis CKD.

Public health implications

Although exploration of the mechanisms that underlie susceptibility to renal disease in these populations is of the utmost importance for the future, there is a pressing worldwide health care challenge that will accelerate at a pace faster than fundamental research can head off. In the United Kingdom, the overall age-adjusted relative risk remains more than threefold in both the South Asian and African Caribbean populations, and this risk might be increasing. The younger age distribution of the ethnic minority population means even larger future increases in the demand for RRT. Estimates of need are based on the presumption that current acceptance rates are a true reflection of demand; this might not be the case if there exists inequity of access to primary health care or restriction of referral to renal units. Data from the United Kingdom Renal Registry show that a higher proportion of South Asians is referred for nephrology care more than a year before the initiation of RRT than is the case for African Caribbeans or whites (Byrne C et al, unpublished data). Concerns thus remains that late referral (for example, African Caribbean and low-income whites) is a significant factor in a number of poorer and rapidly increasing migrant populations that are at marked socioeconomic disadvantage.

Screening for CKD could present fewer organizational challenges than is sometimes thought. The great majority of patients with CKD will be identified in screening programs among people with diabetes, hypertension, and established cardiovascular disease. Thus, an integrated approach to health care for these populations that share a high cardiovascular risk with CKD should prove cost-effective.

The United Kingdom government's recently published National Service Framework for Renal Services [57]

recognizes the increased risk of ESRD among black and ethnic minority populations, and requires those responsible for health care to meet the needs of these groups in local planning. But vigorous advocacy must continue if resources sufficient to deliver the required standards of care are to be made available where populations include large ethnic minorities. The very high demand for RRT must be met. Although intensive efforts at augmenting transplantation rates from both cadaveric and live donors must continue, a disproportionate requirement for dialysis facilities also will continue. Parallel programs for screening and early intervention must be introduced if the future RRT burden is to be restrained. Also, the delivery of high-quality health care that is linguistically and culturally adequate for ethnic minorities will likely require additional resources compared to the resources needed for majority populations. In other areas of the world, different strategies might be appropriate, with an additional emphasis on prevention and early detection, as provision of universal RRT is economically unrealistic.

Non-government agencies play an important role in this work, both as advocates promoting public awareness and government support, and also by generating and directing research resources. One example is the United Kingdom's National Kidney Research Fund, which has been effective in advocacy [58] and, through its ABLE program (A Better Life through Education and Empowerment), also provides resources such as research programs, investigational models for screening, public and community awareness, and approaches to the education of primary care health professionals. The International Society of Nephrology's Commission for Global Advancement of Nephrology (COMGAN) continues to expand its influence and has been forceful in emphasizing the pressing needs in nephrologic care in many regions of the world. Priority also must be given to the long-term goals of understanding genetic and other factors influencing the susceptibility of ethnic populations to CKD if truly effective preventative strategies are to be achieved.

QUESTIONS AND ANSWERS

DR. JOHN T. HARRINGTON (*Dean Emeritus, Department of Medicine, Tufts University School of Medicine; Division of Nephrology, Tufts-New England Medical Center, Boston, Massachusetts*): I've always been skeptical about the importance of ethnicity and race per se, although there is no doubt that significant differences exist. I would argue, as have others [59, 60], that the differences are largely due to class, which in the United States means income and other financial assets, and that class exerts the more powerful effect. How would you respond to this view?

PROFESSOR FEEHALLY: I would not argue against the hypothesis that social deprivation is a major health factor. These articles indicate that in the United States, class might represent a greater factor than ethnicity as a determinant of health. Some of the other ethnic minority populations I have discussed are also severely socially deprived, for example, the native Australian populations such as the Tiwi, and social deprivation is a feature of many such indigenous or migrant populations, but it is not universal. I work in a city that has a migrant South Asian population that is successful, prosperous, and well educated. Yet this group has an incidence of ESRD three to four times that of the white population. Recent registry data in the United Kingdom also provide evidence that ethnicity and social deprivation are separate but additive influences [36]. In my view, economic deprivation is not the major causative factor in an increase in kidney disease, although it might well be an amplifier of both susceptibility and progression.

DR. HARRINGTON: Are there any data on the health status of the second generation of South Asians in Leicester?

PROFESSOR FEEHALLY: Too few second-generation South Asians born in the United Kingdom have so far developed ESRD to give us reliable data. However, growing evidence of type 2 diabetes in South Asians as well as whites in the United Kingdom underlies a concern that the incidence of ESRD will increase further.

DR. AMINU K. BELLO (*Sheffield Kidney Institute, Sheffield, United Kingdom*): Considering the very high risk of ESRD among the ethnic minorities, do they require a different intensity and/or targets of intervention for better control of risk factors?

PROFESSOR FEEHALLY: We have no evidence that different targets, for example, for glycated hemoglobin or blood pressure, should be used in ethnic minority populations; nor that interventions should differ, for example, the use of ACE inhibitors [39]; nor that the timing of interventions should differ.

DR. BELLO: Are large-scale epidemiologic studies necessary in sub-Saharan Africa and Asia to corroborate the research findings here in the west?

PROFESSOR FEEHALLY: Such studies would be very informative but very difficult to achieve. Studies that use onset of ESRD for case ascertainment will not give any information on true prevalence or incidence in countries where RRT is far from universal, and population-based epidemiologic studies of CKD require infrastructure and resources not available in such countries.

DR. AUDREY GOROVICH (*York Hospital, York, United Kingdom*): Have you considered other factors that might influence the incidence of CKD in Asian populations such as vegetarian diet, traditional herbal remedies, and number of pregnancies in women?

PROFESSOR FEEHALLY: These are all interesting and potentially important factors. Diet has not been directly investigated, but the incidence of ESRD in South Asians

in the United Kingdom does not appear to differ between populations that are vegetarian or omnivorous. In view of the well-known adverse effects of herbal medicine exemplified by Chinese herb nephropathy, traditional medicine should be considered, but at present there is no systematic evidence on this issue. Multiple pregnancies might adversely affect the natural history of ESRD in women who embark on pregnancy once CKD is established, but this has not been systematically studied either.

DR. GOROVICH: Are any comparisons available with economically disadvantaged people of white origin in places like Belarus, Moldavia, or Serbia?

PROFESSOR FEEHALLY: At present, the limited infrastructure for the treatment of ESRD in such countries means that the number of new patients starting RRT is not a reliable guide to the true incidence of ESRD, so such comparative information is not available.

DR. ALKIS PIERIDES (*Nicosia General Hospital, Nicosia, Cyprus*): The patient you discussed had tubulointerstitial disease with mild hypertension and a rapid evolution to ESRD. Please comment on the use of nonsteroidal anti-inflammatory drugs (NSAIDs), which have been incriminated in part in the increased incidence of ESRD.

PROFESSOR FEEHALLY: I agree that NSAID use should be carefully considered when chronic tubulointerstitial disease of otherwise undetermined cause is identified. But I know of no evidence that they particularly cause ESRD or its progression in South Asian patients.

DR. PIERIDES: We recently presented data linking mutations 677TT and 677CT/1298AC in the MTHFR gene in patients with hypertension and a negative urine sediment to the development of ESRD. It would be a worthwhile project to investigate mutations in this gene in different ethnic groups with ESRD.

PROFESSOR FEEHALLY: Yes, thank you for this interesting information. We should consider this among many other candidate polymorphisms that might influence susceptibility to renal disease and its progression.

DR. CHARLES PUSEY (*Imperial College, London, United Kingdom*): John, you mentioned that many ethnic populations have an increased incidence of ESRD compared with European whites. I have two related questions. First, do you think that this increase is due to an increased prevalence of CKD, or could it be due to a faster progression to renal failure? The latter is perhaps suggested by recent data in South Asians from Lightstone and colleagues (Lightstone L, unpublished observation). Second, since many ethnic groups across the world appear to have a higher incidence of ESRD, perhaps we European whites have an unusually low rate. Do you think this group might have some genetic factor that protects them from progression and would be amenable to study in our United Kingdom populations?

PROFESSOR FEEHALLY: We don't have a definitive answer to your question about faster progression in ethnic minorities rather than susceptibility to renal disease per se. But recent data, including that which you mentioned (Lightstone L, unpublished observations) and data from the United States, increasingly favor a predominant effect on progression. It will be important to confirm this point with further data as soon as possible, because it will influence our approach not only to etiologic studies (for example, by restricting the candidate genes we consider) but also to public health planning of early identification and intervention.

On your second point, I am increasingly attracted by the notion that we should reverse our thinking and consider why white populations might be uniquely protected from ESRD, although this is, of course, rather speculative. And we should not assume that the answer will be a genetic distinction. For example, the urban, wealthy and well-fed society in which white Europeans now live has developed over 200 years or so since the Industrial Revolution, whereas many of the ethnic minority populations we are considering have been subjected to such urbanization and dietary changes over no more than one or two generations; we could speculate that the rate of environmental change adversely influences the development of "modern" medical problems, including ESRD.

DR. CHARLIE TOMSON (*Institute for Healthcare Improvement, Boston, Massachusetts*): You described the excellent outcome of live donor transplantation in this patient, and this therapy was clearly the right choice. However, the donor in this case had a family history both of diabetes and of renal failure. What is your approach to preoperative counseling of such potential donors?

PROFESSOR FEEHALLY: This is a difficult problem and one you are right to raise. The donor in this case undoubtedly has an increased risk of developing ESRD in later life. He is South Asian and has a family history of ESRD and of type 2 diabetes. But at present, we do not have sufficient information to be able to quantify the future risk of this individual who we know is without clinical renal disease in young adult life since he has been through a live donor evaluation. In the absence of such numeric data, our approach is to rigorously counsel potential donors in broad terms about the risks. But as we all know, the individual desire of the donor and the family dynamics create a powerful drive toward donation despite such increased risks.

DR. CHRISTOPHER G. Winearls (*Oxford Radcliffe Hospital, Oxford, United Kingdom*): Why are there large variations in the incidence of ESRD in populations of European origin, for example, England, North America, Australia, Belgium, and Germany?

PROFESSOR FEEHALLY: A very important question and in my view we do not yet properly understand these differences. It seems improbable that these variations are

the consequence of major genetic differences or environmental factors, but some interaction of these two, particularly as it influences susceptibility to type 2 diabetes, might be important.

DR. GWYN WILLIAMS (*Guy's Hospital, London, United Kingdom*): If we are to achieve our aim of increasing education and awareness about renal disease in ethnic minority populations, we must convince the United Kingdom and local governments of the importance of the issue and also involve the local "government" of the National Health Service, including the hospital Trusts, Foundation Hospitals and Primary Care Trusts.

PROFESSOR FEEHALLY: I agree it can be a problem engaging National Health Service administrative machinery to ensure that the issue is given high priority in health planning. We are particularly fortunate where I work in Leicester because one Primary Care Trust is responsible for the health care of a large proportion of our South Asian population, and the Trust is seriously committed to these issues. But this is not just an issue for ethnic minority people at high risk; the need to improve understanding of CKD and its early detection and management affects the entire population. Part 2 of the National Service Framework for Renal Services in England (February 2005) will cover these issues and give an important opportunity for promoting these matters across the whole health community.

DR. JEREMY DUFFIELD (*Department of Renal Medicine, Brigham & Womens Hospital, Boston, Massachusetts*): What you have described today is a unifying model for ESRD in humans, as all causes of renal disease are over-represented in your South Asian patients. I would argue strongly that these patients must be enrolled in a genetic study to identify the key genes regulating progression.

PROFESSOR FEEHALLY: You will not be surprised to hear that I agree with you. But such a genetic study is not entirely straightforward. For example, it is possible to define a "control" as an individual who at the time of study has not yet developed CKD, but in a high-risk population, this does not exclude the possibility that that individual will do so in the future. Part of the solution is to make such a study as large as possible. There are approximately 2500 people of South Asian origin with ESRD in the United Kingdom at the moment, and we hope we can secure funding for a DNA bank recruiting the great majority of the cohort.

DR. LIZ LIGHTSTONE (*Imperial College, London, United Kingdom*): I have two comments. First, children in ethnic communities, especially of consanguinous marriages, have high rates of renal disease, particularly congenital structural abnormalities. Second, there are difficulties of access to health care for certain ethnic communities, including African Caribbeans in the United Kingdom. There might be less clear routes of access to health care, so management of renal disease in these populations might be more resistant to community intervention. My question is whether there is any evidence from mixed-race populations of dominant protection conferred by "white" genes?

PROFESSOR FEEHALLY: Thank you for your two important comments. I agree with you that community interventions will not always be fruitful. One example in the United Kingdom is the slow progress being made in increasing cadaveric donor rates among ethnic minority populations despite some excellent and innovative educational programs. Access to health care is without doubt variable, and evidence of late referral is emerging from some United Kingdom ethnic minority populations. This problem implies poorer access, for many possible reasons, to specialist renal services [60]. In answer to your question, I know of no such data among mixed-race populations, and I suspect that the major migrations to the United Kingdom have been too recent for such effects yet to be identifiable. But I agree with you that this is potentially a very valuable source of genetic information.

DR. HARRINGTON: Neil Powe, an African American from Washington, DC, who has been interested in these kinds of studies, presented one of our Forums several months ago [41]. Dr. Powe has told me that he did not have any data on the incidence of ESRD in children of black/white parents. At present neither I nor Dr. Powe is aware of such studies.

DR. MICHAEL J. World (*Queen Elizabeth Hospital, Birmingham, United Kindom*): Gurkha recruits to the British army must have no evidence of nephritis at enlistment, but the onset of nephritis was fourfold greater in Gurkhas than in white male British soldiers from 1985 to 1995 (World M, unpublished observations). No significant difference was apparent in the proportions of IgA nephropathy and other types of nephritis between the Gurkhas and Causasoids. I have the clinical impression that the rate of deterioration of IgA nephropathy, at least, is worse in Gurkhas.

PROFESSOR FEEHALLY: That is a very interesting observation in another population that has not, to my knowledge, been studied previously.

DR. PATRICK NAISH (*University Hospital of North Staffordshire, Stoke-on-Trent, United Kingdom*): In light of the known evidence of the influence of sedentary lifestyle on type 2 diabetes, the beneficial effect of increased physical activity, and the difficulty of achieving this change in lifestyle, I would be interested in your comments on this aspect of risk modification.

PROFESSOR FEEHALLY: We know much about exercise, control of energy, and salt intake, all which are important in these high-risk populations. I am conscious as a physician of the very small amount of time I have to influence these issues given the power of advertising, the food industry, and peer pressure influencing lifestyle. But

I agree with you that if we can modify lifestyle to the good and sustain the change for half a century, we will make a major impact on the issues we are discussing.

DR. TERRY FEEST (*Southmead Hospital, Bristol, United Kingdom*): I have two comments. On the question of prevalence and incidence, if progression is faster, then patients leave the stage 3 CKD cohort quicker. If progression is faster in ethnic minorities, and, as you say, the prevalence of stage 3 CKD is the same in whites and ethnic minorities, then the ethnic minorities must be entering the cohort faster. That is, there must also be a higher incidence as well as faster progression. My second comment is that in the Renal Association United Kingdom Renal Registry Report 2003, the effects of social deprivation and ethnicity were separated. There was a small effect of social deprivation in whites that was magnified in the ethnic minorities [36].

ACKNOWLEDGMENT

This Forum was presented at a meeting of the British Renal Association in September 2004.

Reprint requests to Professor John Feehally, The John Walls Renal Unit, Leicester General Hospital, Gwendolen Road, Leicester, LE5 4PW, United Kingdom.
E-mail: jf27@le.ac.uk

REFERENCES

1. FEEHALLY J, BURDEN AC, MAYBERRY JF, *et al*: Disease variations in Asians in Leicester. *Q J Med* 86:263–269, 1993
2. LIGHTSTONE L, REES AJ, TOMSON C, *et al*: High incidence of end-stage renal disease in Indo-Asians in the UK. *Q J Med* 88:191–195, 1995
3. RODERICK PJ, RALEIGH VS, HALLAM L, MALLICK NP: The need and demand for renal replacement therapy in ethnic minorities in England. *J Epidemiol Community Health* 50:334–339, 1996
4. U.S. RENAL DATA SYSTEM: *USRDS 2004 Annual Data Report: Atlas of End-stage Renal Disease in the United States*, Bethesda, MD, National Institutes of Health, National Institutes of Diabetes and Digestive and Kidney Diseases, 2004
5. NARVA AS: Kidney disease in American Indians. *J Natl Med Assoc* 94:738–742, 2002
6. NELSON RG: Diabetic renal disease in transitional and disadvantaged populations. *Nephrology* 6:9–17, 2001
7. SHAH VO, SCAVINI M, STIDLEY C, *et al*: Epidemic of diabetic and non-diabetic renal disease among the Zuni Indians: The Zuni Kidney Project. *J Am Soc Nephrol* 14:1320–1329, 2003
8. HOY W: Renal disease in Australian Aborigines. *Nephrol Dial Transplant* 15:1293–1297, 2000
9. BURDEN AC, MCNALLY PG, FEEHALLY J, WALLS J: Increased incidence of end-stage renal failure secondary to diabetes mellitus in Asian ethnic groups in the United Kingdom. *Diab Med* 9:641–645, 1992
10. NELSON RG, NEWMAN JM, KNOWLER WC, *et al*: Incidence of end-stage renal disease in type 2 (non–insulin-dependent) diabetes mellitus in Pima Indians. *Diabetologia* 31:730–736, 1988
11. KING H, AUBERT RE, HERMAN WH: Global burden of diabetes, 1995-2025: Prevalence, numerical estimates, and projections. *Diabetes Care* 21:296–309, 1998
12. BALL S, LLOYD J, CAIRNS T, *et al*: Why is there so much end-stage renal failure of undetermined cause in UK Indo-Asians? *Q J Med* 94:187–193, 2001
13. EASTWOOD JB, CORBISHLEY CM, GRANGE JM: Tuberculosis and the kidney. *J Am Soc Nephrol* 12:1307–1314, 2001
14. ROSTAND SG, BROWN G, KIRK KA, *et al*: Renal insufficiency in treated essential hypertension. *N Engl J Med* 88:1696–1699, 1989
15. HSU CY, LIN F, VITTINGHOFF E, SHLIPAK MG: Racial differences in the progression from chronic renal insufficiency to end-stage renal disease in the United States. *J Am Soc Nephrol* 14:2902–2907, 2003
16. HOY WE, WANG Z, VANBUYNDER P, *et al*: The natural history of renal disease in Australian Aborigines. Part 2. Albuminuria predicts natural death and renal failure. *Kidney Int* 60:249–256, 2001
17. BUCK K, FEEHALLY J: Diabetes and renal failure in Indo-Asians in the UK—A paradigm for the study of disease susceptibility. *Nephrol Dial Transplant* 12: 1555–1557, 1997
18. CASS A, CUNNINGHAM J, SNELLING P, *et al*: Exploring the pathways leading from disadvantage to end-stage renal disease for indigenous Australians. *Soc Sci Med* 58:767–785, 2004
19. FREEDMAN BI: End-stage renal failure in African Americans: Insights into kidney disease susceptibility. *Nephrol Dial Transplant* 17:198–200, 2002
20. SATKO SG, LANGEFIELD CD, DAEIHAGH P, *et al*: Nephropathy in siblings of African Americans with overt type 2 diabetic nephropathy. *Am J Kidney Dis* 40:489–494, 2002
21. MARCANTONI C, MA LJ, FEDERSPIEL C, FOGO AB: Hypertensive nephrosclerosis in African Americans versus Caucasians. *Kidney Int* 62:172–180, 2002
22. IMPERATORE G, KNOWLER WC, NELSON RG, HANSON RL: Genetics of diabetic nephropathy in the Pima Indians. *Curr Diab Rep* 1:275–281, 2001
23. THE FAMILY INVESTIGATION OF NEPHROPATHY AND DIABETES RESEARCH GROUP: Genetic determinants of diabetic nephropathy: The family investigation of nephropathy and diabetes [FIND]. *J Am Soc Nephrol* 14:S202–S204, 2003
24. JAFAR TH, CHATURVEDI N, GUL A, *et al*: Ethnic differences and determinants of proteinuria among South Asian subgroups in Pakistan. *Kidney Int* 64:1437–1444, 2003
25. NEEL JV, JULIUS S: Type II diabetes, essential hypertension, and obesity as "syndromes of impaired genetic homeostasis": The "thrifty genotype" hypothesis enters the 21st century. *Perspect Biol Med* 64:44–74, 1998
26. CRUICKSHANK JK: Sick genes, sick individuals or sick populations with chronic disease? The emergence of diabetes and high blood pressure in African-origin populations. *Int J Epidemiol* 30:111–117, 2001
27. SPAREN P, VAGERO D, SHESTOV DB, *et al*: Long term mortality after severe starvation during the siege of Leningrad: Prospective cohort study. *Br Med J* 328:11–14, 2004
28. BARKER DJP, HALES CN, FALL CHD, *et al*: Type 2 (non–insulin-dependent) diabetes mellitus, hypertension and hyperlipidaemia (syndrome X): Relation to reduced fetal growth. *Diabetologia* 36:62–67, 1993
29. HUXLEY R, NEIL A, COLLINS R: Unravelling the fetal origins hypothesis: Is there really an inverse association between birthweight and subsequent blood pressure? *Lancet* 360:659–665, 2002
30. MACKENZIE HS, BRENNER BM: Fewer nephrons at birth: A missing link in the etiology of essential hypertension? *Am J Kidney Dis* 26:91–98, 1995
31. KELLER G, ZIMMER G, MALL G, *et al*: Nephron number in patients with primary hypertension. *N Engl J Med* 348:101–108, 2003
32. KONJE JC, BELL SC, MORTON JJ, *et al*: Human fetal kidney morphometry during gestation and the relationship between weight, kidney morphometry and plasma active renin concentration at birth. *Clin Sci* 91:169–175, 1996
33. HUGHSON M, FARRIS AB, DOUGLAS-DENTON R, *et al*: Glomerular number and size in autopsy kidneys: The relationship to birth weight. *Kidney Int* 63:2113–2122, 2003
34. INGELFINGER JR: Is microanatomy destiny? *N Engl J Med* 348:99–100, 2003
35. SINGH GR, HOY WE: Kidney volume, blood pressure, and albuminuria: Findings in an Australian aboriginal community. *Am J Kidney Dis* 43:254–259, 2004
36. RENAL ASSOCIATION UK: *Renal Registry Report 2003*, Bristol, UK Renal Registry, 2003
37. TARVER-CARR ME, POWE NR, EBERHARDT MS, *et al*: Excess risk of chronic kidney disease among African-American versus white

subjects in the United States: A population-based study of potential explanatory factors. *J Am Soc Nephrol* 13:2363–2370, 2002
38. Lakkis J, Weir M: Pharmacological strategies for kidney function preservation: Are there differences by ethnicity? *Adv Renal Replace Ther* 11:24–40, 2004
39. Agodoa L: Lessons from chronic renal disease in African Americans: Treatment implications. *Ethn Dis* 13:S2-118–S2-124, 2003
40. Hoy WE, Baker PR, Kelly AM, Wang Z: Reducing premature death and renal failure in Australian Aboriginals. A community-based cardiovascular and renal protective program. *Med J Aust* 172:473–478, 2000
41. Powe N: Nephrology Forum: To have and have not: Health and health care disparities in chronic kidney disease. *Kidney Int* 64:763–772, 2003
42. Kotchen JM, Shakoor-Abdullah B, Walker WE, *et al*: Hypertension control and access to health care in the inner city. *Am J Public Health* 88:1696–1699, 1998
43. Steel J, Ellis P: Do demographic variables affect the timing of referral to a nephrologist? *EDTNA ERCA J* 28:185–187, 2002
44. Bakewell A, Higgins R, Edmunds M: Nutrition, adequacy of dialysis, and clinical outcome in Indo-Asian and White European patients on peritoneal dialysis. *Q J Med* 95:811–820, 2003
45. Li PKT, Chow KM, Szeto CC: Is there a survival advantage in Asian peritoneal dialysis patients? *Int J Artif Org* 26:363–372, 2003
46. Lo WK, Li FK, Choy CBY, *et al*: A retrospective survey of attitudes toward acceptance of peritoneal dialysis in Chinese end-stage renal failure patients in Hong Kong—From a cultural point of view. *Perit Dial Int* 3:S318–S321, 2001
47. Juergensen PH, Gorban-Brennan N, Troidle L, Finkenstein FO: Racial differences and peritonitis in an urban peritoneal dialysis center. *Adv Perit Dial* 18:117–118, 2001
48. Loucaidou M, Prasad S, Van Trmop J, *et al*: Outcome of renal transplantation in South Asian recipients is similar to that in non-Asians. *Transplantation* 78:1021–1024, 2004
49. Cecka JM: The UNOS Renal Transplant Registry. *Clin Transplant* 1–20, 2002
50. Foster CE, Philosophe B, Schweistzer EJ, *et al*: A decade of experience with renal transplantation in African Americans. *Ann Surg* 236:794–804, 2002
51. Ayanian JZ, Cleary PD, Keogh JH, *et al*: Physicians' beliefs about racial differences in referral for renal transplantation. *Am J Kidney Dis* 43:350–357, 2004
52. Haji NI, Nelson RE, Jones MNA, *et al*: Will transplantation of kidneys from donors with blood group A2 into recipients with blood group B help British Indo-Asian patients with renal failure. *Transplantation* 77:630–633, 2003
53. Roberts JP, Wolfe RA, Bragg-Gresham JL, *et al*: Effect of changing the priority for HLA matching on the rates and outcomes of kidney transplantation in minority groups. *N Engl J Med* 350:545–551, 2004
54. Bakewell A, Higgins R, Edmunds ME: Does ethnicity influence perceived quality of life of patients on dialysis and following renal transplant? *Nephrol Dial Transplant* 16:1395–1401, 2001
55. Lopes AA, Bragg-Gresham JL, Satayathum S, *et al*: Health-related quality of life and associated outcomes among hemodialysis patients of different ethnicities in the United States: The Dialysis Outcomes and Practice Patterns Study. *Am J Kidney Dis* 41:605–615, 2003
56. Thomas CJ: The context of religiosity, social support and health locus of control: Implications for the health-related quality of life of African-American hemodialysis patients. *J Health Soc Policy* 16:43–54, 2002
57. The National Service Framework for Renal Services: Part One: *Dialysis and Transplantation*, Department of Health, 2004
58. Lightstone L: *Preventing Kidney Disease: The Ethnic Challenge*, National Kidney Research Fund, 2001
59. Pincus T: Will racial and ethnic disparities in health be resolved primarily outside of standard medical care? *Ann Intern Med* 141:224–225, 2004
60. Isacs SL, Schroeder SA: Class—The ignored determinant of the nation's health. *N Engl J Med* 353:1137–1142, 2004