Toward understanding chronic kidney disease in African Americans

Randomized trials sit at the pinnacle of the clinical research pyramid. Yet for decades we have recognized that a specific therapy given to an individual patient in the real world may not have the result observed in a clinical trial. Trial medicine differs from real-world medicine in many ways, including rigorous attention to monitoring for compliance and safety. In addition, historically, volunteers have differed from real-world patients in several obvious ways, including demographics. For years, many cardiovascular trials in the United States were performed in populations of limited diversity, lacking appropriate numbers of women, Asians, and African Americans.

Clinical experience and observational studies made us aware that African American patients responded differently to some treatments than the white male patients in the clinical trials. This awareness led to some interesting biologic hypotheses and, over the past 13 years, has led to trials focused on the treatment of heart failure and hypertension in African Americans. But a full biologic understanding of the apparent racial differences in clinical response to specific therapies has for the most part remained elusive.

Contributing to this understanding gap was that we historically did not fully appreciate the differences according to race (and likely sex) in the clinical progression of diseases such as hypertension, heart failure, and, as discussed in this issue of the *Journal* by Dr. Joseph V. Nally, Jr. (page 855), chronic kidney disease. African Americans with congestive heart failure seem to fare worse than their white counterparts with the same disease. Given the strong link between heart failure and chronic kidney disease and the crosstalk between the heart and kidneys, it is no surprise that African Americans with chronic kidney disease progress to end-stage renal disease at a higher rate than whites. Yet, as Dr. Nally points out, once on dialysis, African Americans live longer—an intriguing observation that came from analysis of large databases devoted to the study of patients with chronic kidney disease.

As a patient's self-defined racial identity may not be biologically accurate, using molecular genetic techniques to delve more deeply into the characteristics of patients in these chronic kidney disease registries is starting to yield fascinating results—and even more questions. Links between *APOL1* gene polymorphisms and the occurrence of renal disease and the survival of transplanted kidneys is assuredly just the start of a journey of genomic discovery and understanding.

Readers will note the short editor's note at the start of Dr. Nally's article, indicating that it was based on a Medicine Grand Rounds lecture at Cleveland Clinic, the 14th annual Lawrence "Chris" Crain Memorial Lecture. In 1997, Chris became the

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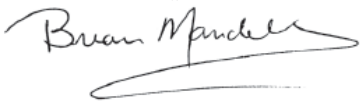
first African American chief resident in internal medicine at Cleveland Clinic, and I had the pleasure of interacting with him while he was in that role. Chris was a natural leader. He was soft-spoken, curious, and passionate about delivering and understanding the basics of high-quality clinical care.

After his residency, with Byron Hoogwerf as the internal medicine program director, Chris trained with Joe Nally as his program director in nephrology, and further developed his interest in renal and cardiovascular disease in African Americans. He moved to Atlanta, where he died far too prematurely in July 2003. That year, in conjunction with Chris's mother, wife, extended family, and other faculty, Drs. Hoogwerf and Nally established the Lawrence "Chris" Crain Memorial Lectureship, devoted to Chris's passion of furthering our understanding and our ability to deliver optimal care to African American patients with cardiovascular and renal disease.

I am pleased to share this lecture with you.



BRIAN F. MANDELL, MD, PhD
Editor in Chief