Albuminuria: Marker or Target in Indigenous populations

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Background
Australian Aborigines in remote areas are experiencing an epidemic of renal disease, type 2 diabetes, hypertension, and cardiovascular disease. Adult deaths are increased 3- to 6-fold, and renal failure more than 20-fold. Renal disease is marked by albuminuria. We describe its distributions and correlations in two remote communities in the Northern Territory.

Methods
Observations in Community 1 included a screen of 939 adult participants (18+ years, 90% recruitment), a treatment program, and 8 to 11 years of follow-up. In Community 2, a screen of 259 people, or 60% of adults, included HbA1c, homocysteine, C-reactive protein (CRP), CMV serology, and carotid intimal media thickness (CIMT). Albumin/creatinine ratio (ACR) was measured by immunoassay in g/mol on random urine, with microalbuminuria defined as 3.4 to 33, and overt albuminuria as ACR 34+.

Results
Dipstick urine protein trace + correctly classified 76% of people with ACR 3.4+, and dipstick protein 1+ correctly classified 82% of people with ACR 34+. ACR was stable to glucose loading and water diuresis in subsets of people in Community 1. ACR levels rose steeply with age. Rates of micro- and overt albuminuria in Community 1 were 28% and 21%, and in Community B were 31% and 13%. ACR correlated inversely with estimated glomerular filtration rate (GFR). ACR also correlated directly with weight, blood pressure, cholesterol, triglycerides, random glucose, HbA1c, homocysteine, and GGT levels, and inversely with HDL cholesterol. ACR correlated with skin sores, scabies, high titer antibodies to Helicobacter pylori, high-titer CMV antibodies, with CRP over a greatly elevated range and, inversely, with birth weight. Finally, ACR correlated with CIMT. Baseline ACR predicted loss of GFR over time. ACR 3.4+ predicted all-cause and cardiovascular hospitalization, while ACR 34+ predicted all renal failure developing over 11 years and all-cause natural deaths and cardiovascular disease deaths. ACEi treatment for people with ACR 34+ reduced renal failure and natural deaths, but the hierarchical effect of higher ACRs within that group for renal and nonrenal deaths was maintained.

Conclusion
Random urine ACR is a stable and robust marker of renal disease, which is multideterminant. A broad base of shared risk factors probably explains the simultaneous emergence of the excessive renal and nonrenal chronic disease morbidities from which these populations suffer. Thus, albuminuria is a unifying marker for the harmful effects of the spectrum of chronic disease, and perhaps beyond. Dipstick urine protein is a useful surrogate for ACR when resources are constrained and disease burdens high.

Keywords:
cardiovascular disease, chronic kidney disease, diagnosis and treatment