COMMENTS AND RESPONSES

Response to Comment on: Cherney and Sochett. Evolution of Renal Hyperfiltration and Arterial Stiffness From Adolescence Into Early Adulthood in Type 1 Diabetes. Diabetes Care 2011;34:1821–1826

We thank Drs. Lim and Tan for their interesting comments (1) regarding our article (2). First, we agree that the adrenomedullin (ADM) is an intriguing candidate that may be involved in the pathogenesis of diabetes-related vascular dysfunction as suggested by Lim et al. (3) and others (4). In terms of the relationship between hyperfiltration and ADM, we are only aware of experimental data by Hiragushi et al. (4). This group of investigators reported that streptozotocin-induced diabetic rats exhibited glomerular hypertrophy and increased ADM peptide levels and mRNA expression in afferent arteriole and glomerular tissue. Interestingly, the excretion of nitric oxide (NO) metabolites was also elevated (4). Finally, ADM antisense oligodeoxynucleotides suppressed ADM and NO production. The authors suggested that ADM may promote diabetic microangiopathy, including renal hyperfiltration, through increased endothelial NO synthase production and afferent vasodilatation. These observations have been difficult to translate into humans because the ADM system cannot be directly and specifically inhibited in humans. While we agree that the use of neutral endopeptidase inhibitors in diabetes may yield interesting physiological data, we would expect the higher ADM levels and vasodilatation associated with these agents to worsen hyperfiltration and possibly accelerate the development of nephropathy, similar to the observations made by Corti et al. (5).

We also appreciate the insights made by Lim and Tan with regard to changes in radial augmentation index (AIx) over time in our cohort. Aside from possible effects of the renin-angiotensin system and height on AIx over time, we also reported lower AIx values in hyperfiltering compared with normofiltering patients (2). Although the mechanism responsible for the lower AIx remains unknown, we have suggested that this may be due to increased NO bioactivity. Data from nondiabetic individuals has suggested that ADM is associated with high arterial compliance, although this remains controversial (6). Existing data therefore suggest that the ADM pathway provides an attractive unifying mechanism linking early renal and systemic hemodynamic vasodilatation leading to hyperfiltration and low AIx. Despite practical difficulties limiting human physiology studies in this area, the role of ADM remains interesting and should be examined in future work.

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