COMMENTS AND RESPONSES

Comment on: Sun et al. Protection From Retinopathy and Other Complications in Patients With Type 1 Diabetes of Extreme Duration: The Joslin 50-Year Medalist Study. Diabetes Care 2011; 34:968–974

We were interested to read the recent article in *Diabetes Care* by Sun et al. (1) showing that higher levels of certain advanced glycation end products (AGEs) were inversely correlated with the progression of retinopathy in individuals with long-standing type 1 diabetes. The data appear potentially consistent with an inverse relationship we recently noted between skin intrinsic fluorescence (SIF), a marker of collagen AGEs, and retinopathy also in those with long-standing type 1 diabetes.

SIF was measured using the Scout device (375 nm excitation, 441–496 nm emission window, intrinsic correction coefficients $\kappa_x = 0.6$, $\kappa_m = 0.2$) on the left volar forearm of 106 participants with type 1 diabetes from the Pittsburgh Epidemiology of Diabetes Complications (EDC) study (mean age 48.9 years; mean diabetes duration 40.0 years) (2). Retinopathy was determined by stereo fundus photographs and was graded according to the Early Treatment of Diabetic Retinopathy Study (ETDRS) scale. SIF demonstrated a linear relationship with the severity of retinopathy over the range of background to proliferative diabetic retinopathy ($P < 0.0001$). However, those who had no evidence of retinopathy had the highest SIF values (none vs. background, $P = 0.001$; none vs. advanced, $P = 0.02$; none vs. proliferative diabetic retinopathy/laser, $P = 0.19$; overall Spearman correlation = 0.34, $P = 0.0004$). Our findings are similar to the findings by Sun et al. (1) in that this is a very select subgroup that has experienced an average of 41 years (range 31.2–49.4 years) of diabetes without any retinopathy.

As Monnier et al. (3) pointed out 25 years ago, high fluorescence values in the absence of complications in individuals with long-standing type 1 diabetes suggests that some patients are "resistant to the effect of poor metabolic control." Our participants with high SIF values but who remained free of retinopathy after an average of 41 years of diabetes had better average glycemic control (18-year average updated mean HbA_{1c}) compared with the rest of the population (8.2 vs. 8.8%, $P = 0.02$). This appears to suggest that the resistance observed in the EDC study was to the effects of elevated AGEs, rather than poor metabolic control, as it relates to diabetic retinopathy. The elevated levels of AGEs in these highly selective, small subgroups (five participants in the EDC study and four participants in the Joslin Medalist Study) appear to identify an intriguing minority who are resistant to the effects of AGEs—and potentially glycemia in general—and are deserving of further research.

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References

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