Table 1—*Simple correlation analysis between endothelium-dependent and independent vasodilatation and sTNFR1 and sTNFR2*

	EDVD (%)			EIVD (%)		
	NGT	IGT	Total	NGT	IGT	Total
n	70	30	100	70	30	100
Log_{10} sTNFR1 (ng/ml)	$r = 0.291$, $P = 0.02$	$r = -0.043$, P = NS	$r = 0.107$, P = NS	$r = -0.132$, P = NS	$r = -0.313$, P = NS	$r = -0.178$, P = NS
Log_{10} sTNFR2 (ng/ml)	$r = -0.028$, P = NS	$r = -0.366$, $P = 0.047$	$r = -0.190$, $P = 0.058$	$r = -0.013$, P = NS	$r = 0.171$, P = NS	$r = -0.065$, P = NS

vasodilatation in subjects with IGT described here.

Sustained upregulation of human TNFR2 in transgenic mice leads to a chronic accumulation of cell surface and plasma receptor (9), providing them the capacity to be hyperresponders to circulating TNF-α. It is tempting to speculate that similar findings in subjects with IGT may contribute to both insulin resistance and endothelial dysfunction induced by TNF-α.

In summary, we found divergent associations between both sTNFR and endothelium vasodilatation. The knowledge of how these interactions occur may have therapeutic implications.

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COMMENTS AND RESPONSES

Race Differences in Long-Term Diabetes Management in an HMO

Response to Adams et al.

Adams et al. (1) examined longitudinal differences in HbA_{1c} (A1C) between black and white diabetic members of an HMO. They found a small, but persistent, increase in A1C values in black subjects; however, there is an important omission in their study. There is no indication that the authors considered the potential effect of the presence of variant hemoglobins in the study subjects. Eight percent of black individuals are carriers of hemoglobin S (2) and are thus heterozygotes for an amino acid substitution in the hemoglobin β chain, which can alter A1C test results. The prevalence of this hemoglobinopathy in white Americans is much lower (3). A1C can give an inaccurate assessment of glycemia in patients with sickle hemoglobin. The magnitude of this perturbation is method dependent and is not linear over the entire glycohemoglobin range (4). The possible contribution of this effect to the observed differences in A1C described between black and white patients should have been considered. Failure to be aware of this can result in overtreating these patients, placing them at increased risk of hypoglycemia.

There are some test kits in commercial use that may eliminate interference by hemoglobin variants (5). The authors have not indicated, however, which assay method they used. Without this information and with no correlating blood glucose data, the presumption of racially based "psychosocial barriers to therapy intensification among patients and clinicians" (1) may be unwarranted.

Our efforts to achieve the best possible clinical outcome for our patients with diabetes by near normalization of blood glucose often focus on maintaining A1C levels as near normal as possible without undue hypoglycemia. While A1C is a valuable surrogate for glycemic control, current American Diabetes Association Clinical Practice Recommendations remind us that "[g]lycemic control is best judged by the combination of the results of the patient's SMBG testing and the current A1C result" (6).

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C.B.H. has received honoraria from Sanofi Aventis, Novo Nordisk, GlaxoSmithKline, Takeda, and Eli Lilly.

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Race Differences in Long-Term Diabetes Management in an HMO

Response to Hart

We read Dr. Hart's (1) response to our article with great interest. The issue of racial differences in the presence of variant hemoglobins that may affect HbA_{1c} (A1C) test results is certainly an important one. Ours (2) was a retrospective analysis using electronic medical record data that did not contain information on either the presence of sickle hemoglobin or the results of patient self-monitoring of blood glucose (SMBG) testing. However, because we found persistent differences in A1C lab values by race, even when controlling for individual-level A1C at baseline in our multivariate analyses, we do not believe the presence of sickle hemoglobin in 8% of our population would eliminate the racial disparities we observed. Still, the issue of measurement raised by Dr. Hart is worthy of discussion. Because of possible variations in the calculation of A1C over time, we ran several diagnostic tests on our A1C measures to test for systematic differences in measurement over time by race. While we did not identify shifts in A1C by race, we did find a shift in A1C values for the entire cohort midway through our study period due to a change in the calculation of A1C by an external vendor. As stated in our article (2), we adjusted for this change using statistical techniques and found no race-based differences in the effect of this adjustment.

We agree with Dr. Hart that a combination of patient SMBG and A1C results represents a better standard for assessing actual control. Unfortunately, rates of SMBG testing in this population were below optimal and were particularly low for black patients. Furthermore, information from patient SMBG is not consistently recorded in the medical record. For this reason, we are now exploring strategies for increasing SMBG among all diabetic patients, especially black patients. We are also exploring interventions that would incorporate patient data from both lab A1C testing and SMBG values in clinical decisions.

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Testing the Accelerator Hypothesis: Body Size, β-Cell Function, and Age at Onset of Type 1 (Autoimmune) Diabetes

Response to Dabelea et al.

The contribution by Dabelea et al. (1) to the growing debate on the accelerator hypothesis is an important one, but I wonder if there is a confounder that has not been accounted for in the reasoning. The report revolves principally around Fig. 2, which shows, after appropriate adjustments, a clear inverse relationship between age at diagnosis and BMI (the acceleration predicted) among those whose fasting C-peptide (FCP) levels lay below the median, but none among those whose FCP lay above. The difference is interpreted to mean that any relationship to insulin resistance applies only to a subset of type 1 diabetic children with low β-cell reserve.

The accelerator hypothesis argues that "type 1 and type 2 diabetes are the same disorder of insulin resistance, set against different genetic backgrounds" (2). It predicts a general inverse relationship between BMI (surrogate for insulin resistance) and age at diagnosis and identifies three accelerators that determine the rate at which the β-cell mass declines during life: constitution (genes/gestation), insulin resistance (lipotoxity and antigenicity), and immune response (HLA) genotype (response to insulin resistance–induced antigenicity).

The one adjustment that was not made to the regressions in Fig. 2 of Dabelea et al.'s report may be the crucial one: the HLA genotype. Those children who