We report a boy with relapse of diabetes after 82 months (6.8 years). This boy was hospitalized with severe D+HUS when he was 6 years old. During his stay in the intensive care unit, he developed hyperglycemia and was treated with insulin during 21 days. Eighty months later he presented with nose obstruction and headache and was diagnosed with sinusitis and polyposis nasi. He was treated with antibiotics, but the complaints persisted. Two months later, he was operated on (functional endoscopic sinus surgery), and postoperatively he received 2 mg betamethason for 5 days. On the 5th day, he presented in the emergency department with polyuria, polydipsia, and lethargy. His glycemia was 1,500 mg/dl, and his blood pH was 7.33. He was intravenously treated with insulin, and the corticosteroids were ceased.

To differentiate between type 1 diabetes, glucocorticoid-induced diabetes, and post-HUS diabetes, some additional blood tests were done. Pancreatic autoantibodies, including islet cell, insulin, GAD65, and insulinoma-associated protein 2 antibodies were all negative. Insulin was 4 mU/l for a glycemia of 1,453 mg/dl. After normalization of the glycemia, the boy was started on a basal-bolus regimen with insulin aspart and insulin glargine. Twenty months later, he still requires insulin ($0.5 \text{ units} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$) and has an HbA_{1c} of 6.8%.

Our report in which we describe a relapse of diabetes after 82 months confirms the conclusion of Suri et al. that survivors of D+HUS should have aggressive surveillance and treatment of hyperglycemia, not only in the acute phase but also in the long run.

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Maternal Age and Prevalence of Gestational Diabetes Mellitus

Maternal age is an established risk factor for gestational diabetes mellitus (GDM), but there is no consensus on the age above which there is significantly increased risk of GDM. In the literature, the lowest cutoff is ≥25 years, as recommended by the American Diabetes Association (1), but there are little data to support this recommendation. To determine the age threshold for increased risk of GDM, we have reviewed the prevalence of GDM, diagnosed by the World Health Organization criteria (2), in the singleton pregnancies managed in our department from 1998 to 2001. Data on maternal anthropometric parameters, parity status, and risk factors for GDM such as booking weight ≥70 kg, BMI ≥25 kg/m², chronic hypertension, significant medical history, and smoking, as well as risk factors identified in our population that included carrier of thalassemia trait (3) and HBsAg (4) and presence of iron deficiency anemia, which reduces the risk of GDM (5), were retrieved from a computerized database. The pregnancies were categorized according to maternal age, i.e., ≤20 years, 20–24 years, 25–29 years, 30–34 years, 35–39 years, and ≥40 years, for statistical analysis (SPSS for Windows version 11.0; SPSS, Chicago, IL) using the χ^2 test and Pearson's correlation. Multivariate analysis was used to determine the role of advancing maternal age adjusting for the other significant associated factors, and the adjusted relative risk and 95% CI was calculated for each age cohort with the 20–24 years cohort as the reference.

Of the 16,383 women managed in this period, 15,827 (96.6%) women continued their pregnancies beyond the first trimester, and the number (% of total) from the youngest to the oldest cohort were 318 (2.0%), 1,713 (10.8%), 4,446 (28.1%), 5,457 (34.5%), 3,279 (20.7%), and 614 (3.9%), respectively. There was a significant difference and positive correlation in the prevalence of GDM, increasing from 1.3, 2.5, 6.2, 10.3, 21.7, and 31.9%, respectively, from the youngest to the oldest cohort (P < 0.001). On multivariate analysis and adjusting for significant confounding factors that included weight ≥70 kg, BMI ≥25 kg/m², HBsAg carrier, thalassemia trait carrier, significant medical history, multiparity, smoker, and absence of iron deficiency anemia, the risk for the older cohorts was significantly increased as follows: 25–29 years, 2.59 (1.84–3.67); 30–34 years, 4.38 (3.13–6.13); 35–39 years, 10.85 (7.72–15.25); and ≥40 years, 15.90 (10.62–23.80). There was no significant difference for the <20 years cohort.

Our finding indicates that the risk of GDM becomes significantly and progressively increased from 25 years onwards. This supports the American Diabetes Association recommendation on the use of age ≥25 years as the cutoff for screening and the observation that maternal age ≥25 years is the factor most predictive of GDM (6). In clinical practice, maternal age of ≥25 years should be adopted instead of ≥35 years or 40 years as a risk factor for the development of GDM.

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Maternal Weight Gain Is Associated With Infant Insulin Concentrations During the 1st Year of Life

Since hyperinsulinemia tracks from childhood to adulthood and is associated with diabetes risk, identifying modifiable conditions during gestation that may impact insulin metabolism in offspring is important. We conducted a pilot study to investigate associations between maternal weight gain and infant insulin concentrations in an underserved population at high risk for diabetes. Mexican or Native American women with an infant <1 year of age provided written consent. Infant weight-for-age Z scores (WAZ) were calculated, and nonfasting plasma samples were analyzed for insulin by standard assay. Pearson's bivariate test was used to assess relationships between variables, and the unpaired *t* test was used to examine differences between means.

A total of 16 women ([means ± SE] 21.8 ± 1.7 years) and their infants (6.4 ± 0.9 months; 9 males and 7 females) completed the study, and medical records were available for 9 of these pairs. Based on combined self-reports and medical records, the mean prepregnancy weight was 71.5 ± 4.0 kg, and the mean pregnancy weight gain was 10.7 ± 2.4 kg. Infants were full term with birth weights ranging from 2,495 to 4,309 g (3,381 ± 121.0 g); WAZ scores averaged 0.47 ± 0.23. Blood insulin concentrations averaged 11.5 ± 1.6 mU/l. Gestational weight gain was significantly correlated to infant insulin concentrations ($r = 0.662$; $P = 0.005$); however, for nondiabetic women with verifiable pregnancy weight gain ($n = 8$), this association was strengthened ($r = 0.763$, $P = 0.028$; Fig. 1). Infant insulin concentrations ($n = 16$) were not associated with birth weight, infant age, WAZ scores, prepregnancy weight, or maternal age.

These data show that maternal weight gain predicted infant insulin concentrations, explaining nearly 60% of the vari-
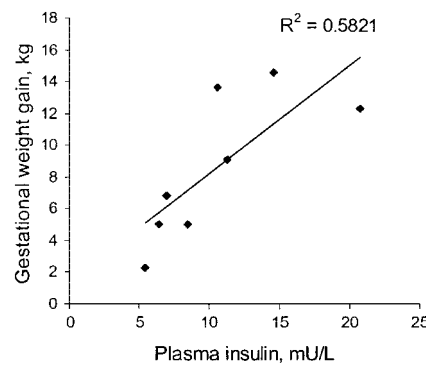
Figure 1—*Correlation of maternal weight gain and infant insulin concentrations (n = 8 mother/infant pairs; r = 0.763, P = 0.028).*

ance in these values. Diabetes during pregnancy has been associated with cord blood insulin and with insulin concentrations in adolescence (1), and in nondiabetic pregnancies, maternal weight gain was related to cord blood insulin in macrosomic neonates (2). Currently, a weight gain of 6.8–11.5 kg is recommended for overweight women, and obese women are advised to gain a minimum of 6.8 kg. In obese, nondiabetic women, minimal gestational weight gain (<5 kg) normalized obstetric outcomes, including hypertension, cesarean section, induction of labor, and macrosomia, and did not adversely affect fetal outcomes (3). Utilizing an emerging obstetric outcome, infant insulin concentrations, our preliminary data support the contention that gestational weight gain should be carefully considered in overweight populations at high risk for diabetes. Differential analyses of our data show that minimal gestational weight gain in the nondiabetic women (≤5 vs. >5 kg) was associated with lower infant insulin concentrations (7.2 ± 0.6 vs. 13.4 ± 2.0 mU/l; $P = 0.013$). Together, the available data indicate that controlling weight gain during obese pregnancies may be advantageous and that more studies of this nature are warranted.

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Soluble Tumor Necrosis Factor Receptor 1 Is Strongly and Independently Associated With Serum Homocysteine in Nonobese Japanese Type 2 Diabetic Patients

The major clinical consequence of type 2 diabetes is mortality and morbidity from atherosclerotic vascular disease. With regards to the risk factors responsible for the evolution of atherosclerosis, Bierman (1) estimated that typical risk factors, including smoking, cholesterol, and blood pressure, can account for no more than 30% of excess cardiovascular risk factors in diabetic patients. Thus, other factors seem to play a key role in the progression of atherosclerosis in diabetes.

One potential factor is homocysteine. Homocysteine has been shown to contribute to the development of atherosclerosis in diabetic patients (2). Whereas the deficiencies of folate and vitamin B_{12} lead to hyperhomocysteinemia, these deficiencies alone do not completely account for atherosclerotic changes induced by homocysteine in diabetic patients.

Tumor necrosis factor (TNF) is a potent candidate involved in the pathogenesis of atherosclerosis. Rauchhaus et al. (3) demonstrated that elevated soluble TNF receptor 1 (sTNF-R1) has shown to be predictive of cardiovascular mortality in patients with chronic heart failure. We