

What Is So Bad About a Big Baby?

The most common and significant neonatal complication clearly associated with gestational diabetes is macrosomia: an oversized baby with a birth weight greater than the 90th percentile for gestational age and sex, or a birth weight >2 SD above the normal mean birth weight. If fetal macrosomia associated with maternal diabetes is directly related to maternal glucose levels (1–3), then strategies to prevent hyperglycemia must be devised to treat the diabetic pregnant woman (4). However, not only is the concept that macrosomia is directly related to maternal hyperglycemia considered controversial, but also the notion that normalizing the maternal glucose could prevent macrosomia is hotly debated. In addition, the definition of normoglycemia during pregnancy has not been adequately reported because of difficulty with measuring glucose excursions in the home setting.

The initial attempts to normalize the 24-h glucose profile were all made with hospitalized patients (5). When self-monitoring of blood glucose became available for outpatient surveillance of glucose control (6), normalization programs could be continued at home. However, the number and timing of the blood glucose determinations have not been adequately studied. In addition, reports that macrosomia occurred despite normoglycemia (7) perpetuated the philosophy that it is urgent to deliver the infant early to avoid fetal overgrowth, which was perceived to be unaffected by glycemic control. Perhaps the debate continues because many of the reports claiming that neonatal complications occur despite excellent metabolic control failed to measure postprandial glucose levels (1–3). The Diabetes in Early Pregnancy (DIEP) study was a multicenter trial of type 1 diabetic pregnant women who were compared with normal control women throughout pregnancy, and it was designed to answer questions related to causes of spontaneous abortions and malformations (8,9). In addition, the study also looked at variables associated with macrosomia (1). The DIEP study reported that the 1-h postprandial glucose levels

predicted 28.5% of the macrosomic infants born to diabetic mothers (1). Combs et al. (3) confirmed these findings when they associated macrosomia with higher postprandial glucose concentrations obtained between weeks 29 and 32 of gestation. DeVeciana et al. (2) reported that gestational diabetic women who only monitor preprandial glucose have a 42% risk of macrosomia, whereas those who also monitor glucose 1 h after eating decrease their risk of neonatal macrosomia to near normal or 12%. Demarini et al. (10) added to the evidence that maternal postprandial glucose monitoring is important. They showed that when the postprandial glucose levels of diabetic women were <120 mg/dl, the infants had a significantly lower rate of hypocalcemia than those infants born to diabetic mothers with higher postprandial glucose levels.

The advent of continuous glucose monitoring has only recently been applied to the study of ambient glucose levels in diabetic pregnant women. To date, there is only one report using a continuous glucose sensor in 10 gestational diabetic women (11). That study showed that continuous monitoring detects postprandial glucose elevations not detected by intermittent fingerstick blood glucose determinations (11). Perhaps “macrosomia despite normoglycemia” is in reality “macrosomia because of undetected hyperglycemia.”

To truly settle the controversy as to the impact of hyperglycemia on the outcome of diabetic pregnancies, we need to establish the normal ranges in pregnancy and relate the levels of glycemia in normal pregnancies to the degrees of fetal overgrowth seen in a normal population. The definition of normoglycemia in pregnancy has not been readdressed for over two decades. The two reports combined only studied 20 third-trimester normal pregnant women with hourly glucose determinations over a 24-h period (12,13). Both reports suggested that “normal” maternal glucose levels were lower than nonpregnant glucose levels, and both reported that fasting levels were 55–65 mg/dl, with no blood glucose level >120 mg/dl, even 1 h after a high-carbohydrate meal. Although some clinicians, in an

attempt to minimize the risk of neonatal macrosomia, have used these levels as goals for the treatment of their diabetic pregnant patients, others have recommended waiting until there is more definitive data before taking a risk and increasing the danger of hypoglycemia in an attempt to lower the maternal glucose levels to “normal.” They want confirmatory evidence showing that normal maternal glucose levels are truly this low and that higher blood glucose levels increase the risk of fetal overgrowth.

Finally, we now have evidence based on maternal third-trimester diurnal glucose levels in normal nondiabetic pregnancies, and it shows that these levels are related to fetal growth. The article in this issue of *Diabetes Care* will settle the controversy. Paretti et al. (14) carefully selected 51 women who by all criteria were absolutely normal, i.e., they had term delivery of a single infant with normal fetal growth, normal glucose challenge tests (<135 mg/dl), no obesity, and no hypertension, and they were allowed to have an unmodified lifestyle. These women monitored their blood glucose levels fortnightly from 28 to 38 weeks of gestation, with timed meals at 8:00 A.M., 12 noon, and 8:00 P.M., and blood glucose levels were measured before each meal and 1 and 2 h after meals. (This was in addition to measurements every 2 h in the afternoon and during the night with a remarkable 96.9% compliance!) Fetal parameters were also measured with the greatest of attention; the fetuses were evaluated by ultrasound scan at 22, 28, 32, and 32 weeks of pregnancy. They showed that the overall daily mean glucose is indeed lower than in nonpregnant women: the third-trimester mean fasting glucose level was 56 mg/dl. Most noteworthy was the observation that the mean peak postprandial glucose response occurred at 1 h, and it never exceeded 105.2 mg/dl. This 1-h peak was significantly correlated with fetal abdominal circumference. By 32 weeks there was a positive correlation between fetal abdominal circumference and the 1-h postbreakfast, 1- and 2-h postlunch, and 1- and 2-h postdinner glucose levels. In addition,

