INTRODUCTION

Few diabetic women lived to childbearing age before the advent of insulin in 1922. Until then, less than 100 pregnancies were reported in diabetic women and most likely these women had type 2 and not type 1 diabetes. Even with this assumption, these cases of diabetes and pregnancy were associated with a greater than 90% infant mortality rate and a 30% maternal mortality rate (1,2). As late as 1980, physicians were still counseling diabetic women to avoid pregnancy (3). This philosophy was justified because of the poor obstetric history in 30–50% of diabetic women. Improved infant mortality rates finally occurred after 1980, when treatment strategies stressed better control of maternal plasma glucose levels and once self-blood glucose monitoring and hemoglobin A1c became available to enable better metabolic control in persons with diabetes (3). As the pathophysiology of pregnancy complicated by diabetes has been elucidated and as management programs have achieved and maintained near normoglycemia throughout pregnancy complicated by type 1 diabetes, perinatal mortality rates have become comparable to those of the general population (4).
EFFECT OF HYPERGLYCEMIA ON THE FETUS AND THE MOTHER

Fetal Complications Secondary to Maternal Hyperglycemia

If the mother has hyperglycemia, the fetus will be exposed to either sustained hyperglycemia or intermittent periods of hyperglycemia. Both situations prematurely stimulate fetal insulin secretion. The Pedersen hypothesis links maternal hyperglycemia-induced fetal hyperinsulinemia to morbidity of the infant (2). Fetal hyperinsulinemia may cause increased fetal body fat (macrosomia) and, therefore, a difficult delivery, or cause inhibition of pulmonary maturation of surfactant and, therefore, respiratory distress of the neonate. The fetus may also have decreased serum potassium levels caused by the elevated insulin and glucose levels and may, therefore, have cardiac arrhythmias. Neonatal hypoglycemia may cause permanent neurological damage. The maternal postprandial glucose level has been shown to be the most important variable to impact the subsequent risk of neonatal macrosomia (5). When the postprandial glucose levels are maintained below 120 mg/dL 1 h after beginning the meal, the risk of macrosomia is minimized (5).

There is an increased prevalence of congenital anomalies and spontaneous abortions in diabetic women who are in poor glycemic control during the period of fetal organogenesis, which is nearly complete by 7 wk postconception. A woman may not even know she is pregnant at this time. It is for this reason that prepregnancy counseling and planning is essential in diabetic women of childbearing age. Because organogenesis is complete so early on, if a woman presents to her health care team and announces that she has missed her period by only a few days, there is still a chance to prevent cardiac anomalies by swiftly normalizing the glucose levels. However, potential neural tube defects are probably already established by the time the menstrual period is missed.

Glycosylated hemoglobin (HbA1c) values provide the best assessment of the degree of chronic glycemic control, reflecting the average blood glucose concentration during the preceding 6–8 wk. As a result, measurement of HbA1c can, in early pregnancy, estimate the level of glycemic control during the period of fetal organogenesis. There are two important observations in this regard: (1) HbA1c values early in pregnancy are correlated with the rates of spontaneous abortion and major congenital malformations, and (2) normalizing blood glucose concentrations before and early in pregnancy can reduce the risks of spontaneous abortion and congenital malformations nearly to that of the general population (6–12).

One report compared 110 women who were already 6–30 wk pregnant at the time of referral, with 84 women recruited before conception and then put on a daily glucose monitoring regimen (13). The mean blood glucose concentration was between 60 and 140 mg/dL (3.3 and 7.8 mmol/L) in 50% of the latter women. The incidence of anomalies was 1.2% in the women recruited before conception vs 10.9% in those first seen during pregnancy. Very similar findings were noted in another study: 1.4% vs 10.4% incidence of congenital abnormalities (14). Major congenital malformations, which either require surgical correction or significantly affect the health of the child, are more common in infants of poorly controlled diabetic mothers (15).

The increased rate of spontaneous abortion in poorly controlled diabetic women is thought to be secondary to hyperglycemia, maternal vascular disease, including uteroplacental insufficiency, and, possibly, immunologic factors (7,16). In addition, animal studies suggest that hyperglycemia regulates the expression of an apoptosis