# Blood Glucose Control During Pregnancy

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Pregnant diabetic women represent a unique category of patient in whom diabetic control is most desirable, since even minor degrees of hyperglycemia have adverse effects on the conceptus. In 18 insulin-dependent pregnant diabetic women (White Class B, N = 4; C, N = 5; D, N = 7; and R, N = 2), we have utilized a therapeutic program consisting of intensive patient education, a multiple-component insulin regimen (two to four injections daily), careful dietary control, and meticulous balancing of food, activity, and insulin dosage, monitoring such balance with patient-determined blood glucose measurements four to seven times daily using the Dextrostix/Eyetone system. Our goals for blood glucose management have been to attain fasting levels of 60–90 mg/dl, preprandial levels less than 105 mg/dl, and postprandial levels less than 120 mg/dl, in the absence of significant hypoglycemia. We have been able to attain these goals for most of the period of monitoring in the majority of these patients, while in the others we have achieved marked improvement in diabetic control, although we did not consistently attain our goals. Despite this, there was not infrequent neonatal morbidity, including a 33% frequency of macrosomia, an 11% frequency of significant hypoglycemia, and a 22% frequency of congenital malformation. Nevertheless, all infants survived and are generally healthy, whereas only 38% of 21 previous pregnancies in these same women have eventuated in living offspring. Thus, although further refinement is clearly indicated, it appears that our approach has resulted in improved pregnancy outcome. Patient self-monitoring of blood glucose is a procedure that is relatively simple, practical, acceptable to patients, and facilitates the attainment of glycemic control. DIABETES CARE 3: 69–76, JANUARY-FEBRUARY 1980.

Pregnant diabetic women represent a unique category of patients in whom diabetic control is most desirable. Control of maternal glycemia is the most important factor influencing fetal outcome.[1–7] Fetal glucose levels are a direct function of maternal glucose levels, since glucose is transported across the placenta to the conceptus by facilitated diffusion.[8] When maternal diabetes mellitus is not well regulated and hyperglycemia is present, the fetus will be exposed to either sustained or meal-related intermittent waves of hyperglycemia. As a consequence, albeit by mechanisms that remain unresolved, the fetal pancreatic B-cell adapts to this setting by the induction of glucose-mediated insulin secretion and B-cell hyperplasia.[9,10] The result is prematurely induced and inappropriately sustained or intermittent fetal hyperinsulinemia that parallels the prevailing blood glucose in the mother and fetus.[11] Many of the physical and morbid complications experienced by infants of mothers with diabetes mellitus can be attributed to fetal hyperglycemia and hyperinsulinemia. Thus, fetal hyperinsulinemia can result in increased fetal body fat (macrosomia), accounting for the cherubic appearance of those infants at birth, and possibly complicating vaginal delivery due to dystocia. Fetal hyperinsulinemia may also inhibit the pulmonary maturation processes required for surfactant production and thereby contribute to the increased incidence of respiratory distress syndrome experienced by these neonates.[12] Additionally, a persistence of enhanced responsivity of the fetal B-cell into neonatal life also contributes to the propensity for developing neonatal hypoglycemia once the fetus is removed from a constantly delivered maternal source of glucose.[13,14]

The standards of assessing diabetic control during pregnancy should be the plasma glucose values found in nondiabetic pregnant women. Pregnancy is normally associated with a significant progressive lowering of fasting plasma glucose from a mean of 73 ± 9 mg/dl in early pregnancy to a

mean of 65 ± 9 mg/dl near term.[15] Diurnal plasma glucose values in nondiabetic women rarely exceed 100 mg/dl, except in the first hour postprandially. Mean diurnal plasma glucose normally is 82 ± 5 mg/dl in early pregnancy and 85 ± 5 mg/dl in late pregnancy.[16] Maximum level of plasma glucose in nondiabetic early pregnancy is 107 ± 10 mg/dl and in late pregnancy is 114 ± 8 mg/dl. The range of plasma glucose excursions normally is 37 ± 8 mg/dl in early pregnancy and 47 ± 7 mg/dl in late pregnancy.[16] Thus, our goals for glycemic control in diabetic women during pregnancy are: fasting plasma glucose, 60–90 mg/dl; preprandial plasma glucose less than 105 mg/dl; and postprandial plasma glucose less than 120 mg/dl. Maintenance of such physiologic levels of plasma glucose should be accompanied by aglycosuria, thus rendering urine glucose monitoring inadequate for the documentation of such meticulous control. Therefore, we and others have suggested that blood glucose self-monitoring should permit improved management of glycemia in pregnant diabetic women.[1,17–25] Previous reports have described our preliminary results with this approach.[1,17] This report describes our treatment approach and outcome in 18 consecutive women with pregestational diabetes in whom glycemia was monitored during pregnancy by self-determinations of blood glucose.

TABLE 1
Clinical characteristics of pregnant diabetic women enrolled in blood glucose self-monitoring program

| Patient no. | Age (yr) | Duration of diabetes (yr) | Parity* | Grade of retinopathy | White Class |
|---|---|---|---|---|---|
| 1 | 21 | 11 | 0-0-0-0 | Background | D |
| 2 | 32 | 14 | 0-0-1-0 | Background | D |
| 3 | 35 | 3 | 3-0-3-2 | None | B |
| 4 | 31 | 9 | 0-0-0-0 | None | B |
| 5 | 20 | 8 | 0-0-0-0 | Background | D |
| 6 | 21 | 8 | 0-0-0-0 | None | C |
| 7 | 16 | 6 | 0-0-0-0 | None | D |
| 8 | 23 | 1 | 0-0-0-0 | None | B |
| 9 | 20 | 5 | 0-0-2-0 | None | C |
| 10 | 24 | 20 | 1-1-0-0 | None | D |
| 11 | 28 | 25 | 0-2-2-2 | Background | D |
| 12 | 31 | 14 | 0-0-0-0 | Background | D |
| 13 | 30 | 19 | 0-1-0-1 | Proliferative | R |
| 14 | 26 | 12 | 0-0-0-0 | None | C |
| 15 | 31 | 2 | 2-0-0-2 | None | B |
| 16 | 23 | 18 | 0-0-2-0 | Proliferative | R |
| 17 | 23 | 4 | 1-0-0-1 | None | C |
| 18 | 22 | 6 | 0-0-0-0 | None | C |
| Mean ± SD | 25.4 ± 5.3 | 10.3 ± 6.9 | | | |

* Parity = number of full-term offspring; number of premature offspring; number of abortions or stillbirths; number of living children.

## PATIENTS

Eighteen pregnant diabetic patients underwent continual blood glucose self-monitoring from the time of first encounter during pregnancy until term. The group included patients of White Classes B (N = 4), C (N = 5), D (N = 7), and R (N = 2). The ages, duration of diabetes, parity, retinopathy grades, and White Classes for each of these patients are summarized in Table 1. All these women had normal values of serum creatinine and/or creatinine clearance, and none had significant proteinuria. Nine of the women were primigravida, while the other nine had a total of 21 previous pregnancies, only 38% of which resulted in living offspring.

## METHODS

*Glycemic management.* Our therapeutic program consists of intensive patient education, a diet providing about 300 kcal/day above basal requirements (a total of 36–50 kcal per kg ideal body weight) to achieve a weight gain of 10–12 kg distributed in an appropriate pattern.[26] At least 45% of calories should be in the form of carbohydrate, including at least 200 g and approximately 50 g/day above nonpregnancy needs; 30 g of protein above the nonpregnant allowance; and appropriate vitamins and minerals. Meals are divided into three meals and at least three snacks, with some women requiring two evening snacks if there is a long interval between supper and bedtime. The Exchange Lists for Meal Planning are used to facilitate consistency and regularity of nutrient consumption.

All patients were treated with a multiple component insulin regimen, generally consisting of both regular and intermediate-acting insulin (NPH or Lente) before breakfast and supper. Usually, initial insulin distribution approximated two-thirds of the total daily dose in the morning (divided as one part regular and two parts NPH or Lente) and one-third of the total daily dose in the evening (divided in equal parts between regular and NPH or Lente). Each component of the insulin is then titrated to achieve glycemic control as close as possible to the goals stated above.

Intensive patient education is directed at understanding glycemic control by achieving a balance between food intake, activity, and insulin dosage, and monitoring of such balance.

*Monitoring of diabetes.* Patients were instructed in the measurement of home blood glucose using the Dextrostix/Eyetone system (Ames Company, Elkhart, Indiana). This method uses reagent strips impregnated with glucose oxidase to determine true blood glucose in a drop of capillary blood obtained by fingerstick.[17] The colorimetric change on the reagent strip is electronically quantified. In our hands, capillary whole blood glucose measured with the Eyetone meter has a correlation coefficient of 0.994 and slope of 0.975 when compared

with venous plasma glucose measured by a Beckman glucose analyzer, suggesting that plasma glucose standards can be used for patient-monitored blood glucose.

Patients daily monitor four blood glucose levels—fasting, prelunch, presupper, and bedtime. Also, at least once weekly, patients obtain at least three additional samples 2 h postprandial: breakfast, lunch, and supper. Initially, patients maintain daily telephone contact with the professional staff (physicians and nurse specialists) of the Diabetes Unit, who together with the patient make appropriate adjustments in insulin dosage in an attempt to achieve euglycemia. As the patient becomes more familiar with the adjustment program, an algorithm for insulin dose alterations is developed and telephone contacts with the professional staff can be less frequent. The patient is seen weekly in the Diabetes Unit for full evaluation of diabetes regulation, review of progress, and discussion of any questions that have arisen.

*Antepartum fetal monitoring.* Monthly serial ultrasonography is used to monitor fetal maturity, growth, and size. Fetoplacental function is monitored by a 24-h urinary estriol/creatinine ratio, commenced between 30 and 32 wk gestation twice or thrice weekly to establish a baseline, with daily determinations begun around 37 wk gestation, depending on antepartum hospitalization. Antepartum fetal heart rate monitoring is used as a noninvasive procedure to assess respiratory functional reserve. Weekly nonstress testing (NST) is supplemented by contraction stress testing (CST) as needed to confirm a suspicious NST. All these are accomplished on an outpatient basis. Abnormal results dictate hospital admission and further assessment, depending on gestational age and fetal status.

*Labor and delivery.* Our goal is for spontaneous labor at term and vaginal delivery. Intrapartum fetal cardiotachometry supplemented by fetal blood sampling (via scalp blood) as needed is used for surveillance of the fetus during this vulnerable period. Glycemic control is accomplished by simultaneous continuous infusions of glucose and insulin, monitored by half-hourly blood glucose determinations in the delivery suite, to maintain blood glucose between 60 and 100 mg/dl. The insulin infusion is discontinued at the time of delivery of the conceptus.

## RESULTS

*Glycemic control.* Self-monitoring of blood glucose was conducted by the 18 patients for 8–31 wk, as summarized in Table 2. From the total of 326 wk, records were analyzed for 316 wk, the records of 3 wk having been lost, and those of 7 wk being inaccurate, since the patient was using erroneous techniques. Of the 316 weekly mean fasting glucose values (most representing the mean of six to seven daily glucose values), 195 (62%) were in the target range of 60–90 mg/dl, while 36 (11%) were below target range and 85 (27%) were above. Of 1257 weekly mean preprandial glucose values, 738 (59%)

TABLE 2
Summary of glycemic control results of self-monitoring program

| Patient no. | Number of weeks monitored | % weeks mean fasting glucose in target range | % weeks mean preprandial glucose in target range | Mean fasting glucose last 3 wk (mg/dl) | Mean preprandial glucose last 3 wk (mg/dl) | Total insulin dose at term (units/day) |
|---|---|---|---|---|---|---|
| 1 | 10 | 60 | 60 | 95 | 98 | 108 |
| 2 | 14 | 43 | 30 | 78 | 103 | 98 |
| 3 | 12 | 50 | 31 | 73 | 106 | 125 |
| 4 | 26 | 26 | 33 | 49 | 77 | 66 |
| 5 | 15 | 73 | 48 | 68 | 97 | 65 |
| 6 | 29 | 66 | 81 | 74 | 71 | 64 |
| 7 | 8 | 88 | 81 | 76 | 79 | 63 |
| 8 | 25 | 80 | 62 | 64 | 72 | 55 |
| 9 | 14 | 43 | 70 | 106 | 105 | 93 |
| 10 | 20 | 85 | 69 | 73 | 90 | 84 |
| 11 | 30 | 77 | 49 | 70 | 92 | 100 |
| 12 | 10 | 56 | 57 | 57 | 85 | 93 |
| 13 | 31 | 65 | 52 | 69 | 113 | 125 |
| 14 | 11 | 45 | 52 | 62 | 81 | 92 |
| 15 | 14 | 86 | 86 | 75 | 88 | 138 |
| 16 | 19 | 32 | 47 | 65 | 94 | 99 |
| 17 | 21 | 53 | 79 | 59 | 82 | 101 |
| 18 | 17 | 65 | 68 | 104 | 114 | 103 |
| Mean ± SD | 18.1 ± 7.4 | | | 73.2 ± 15.2 | 91.5 ± 13.3 | 92.9 ± 23.5 |

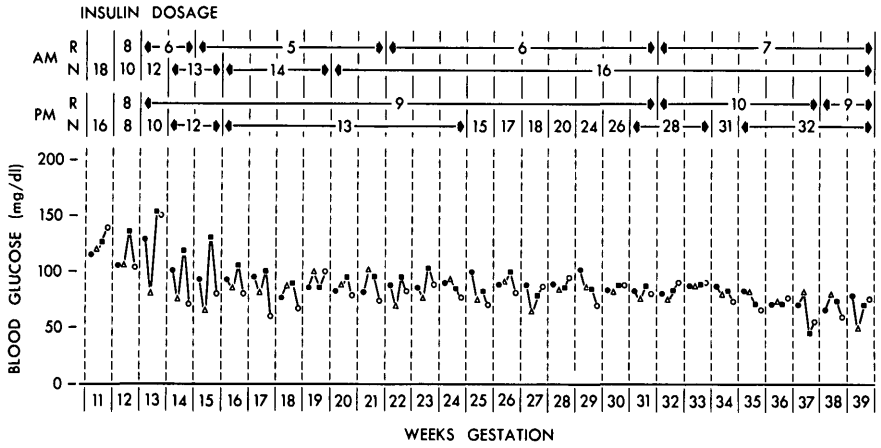


*FIG. 1. Summary of mean weekly preprandial glucose determinations in patient no. 6, a 21-yr-old woman with Class C diabetes. She monitored her blood glucose at home from the eleventh week of gestation until term, and was admitted to the hospital in active labor. Average morning and evening insulin dosage for each week is listed at the top of the figure. Closed circles, mean fasting blood glucose for each week; triangles, mean prelunch blood glucose for each week; squares, mean presupper blood glucose for each week; open circles, mean bedtime (presnack) blood glucose for each week. Each symbol represents four to seven determinations.*

were in the target range, while 98 (8%) were below and 421 (33%) were above. In Table 2 is listed for each patient the percentage of weeks that the weekly mean fasting glucose value and the weekly mean fasting and preprandial glucose values (four per day) were in target range. Also shown in Table 2 is the mean fasting glucose value for the last 3 wk of gestation and the mean value for the same 3 wk of the fasting and preprandial glucose determinations. Also, the total daily insulin dosage at term for each patient is listed in Table 2. We began measuring glycosylated hemoglobin levels late in this project. Four patients had determinations made in the last month of gestation, and all were in the normal (nondiabetic) range for our laboratory. (These were 7.3%, 7.5%, 7.8%, and 7.9%, normal range being 3.0%–8.0%.)

Figures 1–5 are examples illustrating glycemic control throughout pregnancy in five of the patients studied. Figure 6 is an example of glycemic control during labor and delivery.

*Pregnancy outcome.* Mean maternal weight gain was somewhat greater than that recommended,[26] being 14.4 ± 6.4 kg (range 5.5–30 kg). Labor was spontaneous in four women (22%) and induced in eight (44%). Reasons for induction were elective (N = 4), deteriorating glucose control (N = 1), increased blood pressure (N = 1), and nonreactive nonstress test (N = 1). Six women (33%) underwent direct cesarean section without a trial of labor (three of these were repeat cesarean sections, one a breech presentation, one a patient with rising blood pressure, and one an infant with obvious macrosomia in the setting of polyhydramnios). Of the 12 attempts at vaginal delivery, 6 (50%) were delivered successfully, while the other 6 failed to progress and were delivered by cesarean section. Thus, the overall cesarean section rate was 66%, with a primary rate of 50%.

*Infant outcome.* Mean gestational age was 37.6 ± 1.2 wk (range 35–40 wk), as assessed by five separate factors (date of last menstrual period, uterine size, ultrasonography, amniocentesis score, and pediatric assessment of the neonate). Mean birth weight was 3292.8 ± 686.0 g (range 2210–4640 g), with two infants greater than 4000 g in size, although six of the infants (33%) exceeded the 90th percentile in weight for gestational age[27] and were thus considered macrosomic. Only one of these infants showed gross clinical features of macrosomia, however.

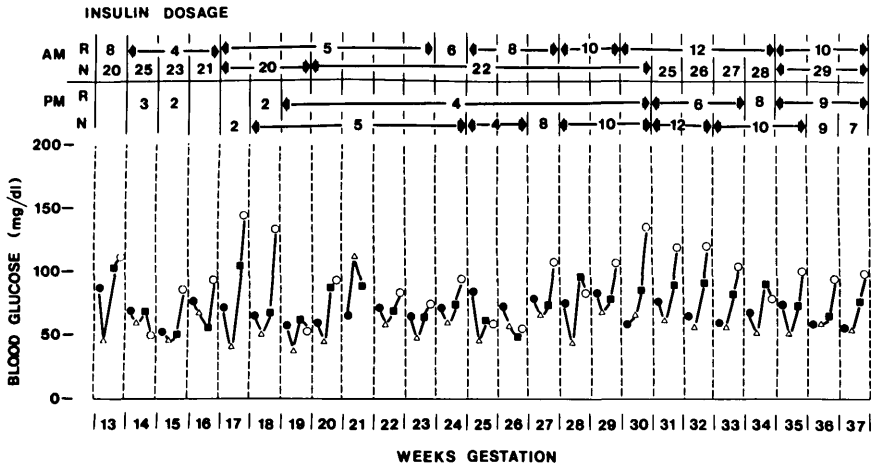


*FIG. 2. Summary of mean weekly preprandial glucose determinations in patient no. 8, a 23-yr-old woman with Class B diabetes. Symbols are the same as in Figure 1.*

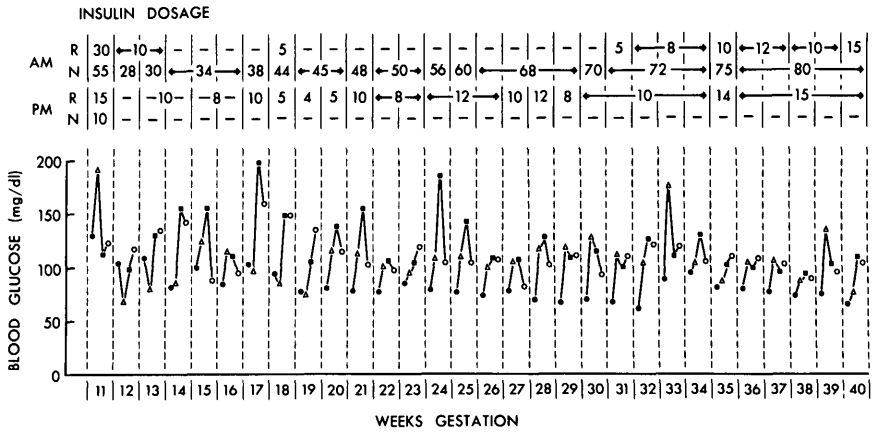


*FIG. 3. Summary of mean weekly preprandial glucose determinations in patient no. 11, a 28-yr-old woman with Class D diabetes. Symbols are the same as in Figure 1.*

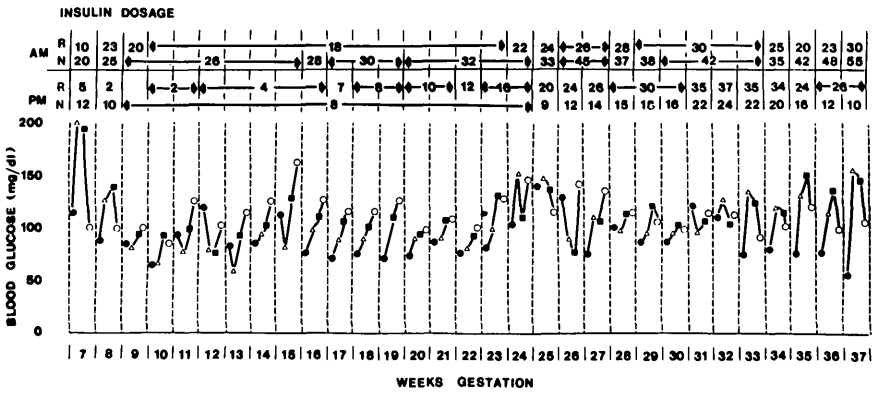


*FIG. 4. Summary of mean weekly preprandial glucose determinations in patient no. 13, a 30-yr-old woman with Class R diabetes and proliferative retinopathy treated by extensive ruby laser and xenon arc photocoagulation at age 23, now with relatively stable, quiescent retinitis proliferans. Symbols are the same as in Figure 1.*

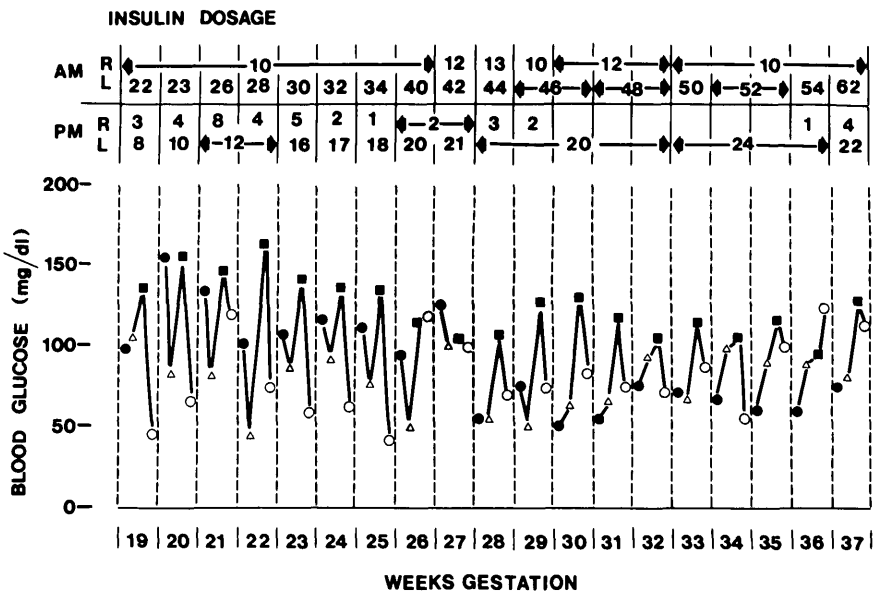


*FIG. 5. Summary of mean weekly preprandial glucose determinations in patient no. 16, a 23-yr-old woman with Class R diabetes and proliferative retinopathy, blind in her right eye from retinal detachment, and with her left eye having undergone extensive argon laser photocoagulation, with resultant scarring and chorioretinitis. Symbols are the same as in Figure 1.*

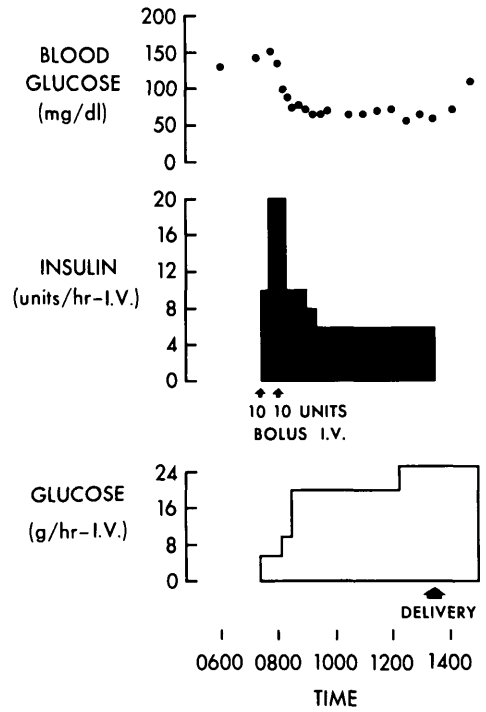


*FIG. 6. Record of insulin and glucose infusion rates and blood glucose responses during labor and delivery for the patient depicted in Figure 1. Glucose infusion rate is 300 μg/kg/h as 5%–10% dextrose in water. Insulin delivery is regulated by infusion pump after an initial intravenous bolus.*

Mean 1-min Apgar score was 8.2 ± 0.9, and mean 5-min Apgar score was 9.1 ± 0.5. The distribution of Apgar scores is shown in Table 3.

Table 4 summarizes overall known infant morbidity. Infants were monitored in the neonatal nursery until discharge. The four congenital malformations include dislocation of the right hip, deafness (detected at age 15 mo), choanal stenosis, and nasal polyps. The latter two malformations were responsible for labored respiration in the neonatal period.

TABLE 3
Distribution of Apgar scores

| Score | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|
| 1-min (N) | 1 | 2 | 8 | 7 | 0 |
| 5-min (N) | 0 | 0 | 1 | 14 | 3 |

## DISCUSSION

Self-monitoring of blood glucose by pregnant diabetic women is a practical and useful tool, which facilitates the attainment of improved glycemic control and the documentation thereof. Although this approach does require intensive effort on the part of both patients and professional staff, along with meticulous attention to details of technique, patients have found it an acceptable approach. In the extremely motivated circumstances of pregnancy, compliance has been excellent. The information collected has served to reassure both the patient and ourselves, and thus has contributed to a decrease in the frequency and duration of hospitalization during pregnancy.

In the small series reported here, glycemic control has been markedly improved and is certainly better than that attained with conventional outpatient approaches, and in many of these women glycemia approximated normal. On the other hand, it is obvious that even with the improved control achieved, there was still significant infant morbidity (Table 4). This can be lessened further with earlier, even more intensive control of glycemia and limitation of maternal weight gain during gestation, as has been shown in the small series reported by Jovanovic and colleagues.[20,21] Yet, all 18 infants in this series survived and are generally healthy, the neonatal morbidity seen being relatively trivial. This is in distinct contrast with the previous pregnancy history in these same women, in which only 38% of pregnancies have eventuated in living offspring.

Although our goal is for vaginal delivery following spontaneous labor at term, we have been able to achieve that goal in only three women, although a fourth entered the hospital for the first time in spontaneous active labor but underwent cesarian section due to inadequate progress of labor. Even these few cases, however, serve to offer us encouragement that our goals can be attained. As we have gained more experience, we have had less reluctance to strive for spontaneous vaginal delivery.

The use of continuous insulin and glucose infusion during labor and delivery, coupled with frequent monitoring of glycemia, has been shown to be both feasible and useful.[1,28] Our

TABLE 4
Infant morbidity

| | N | Percent |
|---|---|---|
| Macrosomia | 6 | 33 |
| Hypoglycemia | | |
| Blood glucose less than 45 | 6 | 33 |
| Blood glucose less than 25 | 2 | 11 |
| Hypocalcemia | 0 | 0 |
| Hyperbilirubinemia | | |
| Day 1 | 0 | 0 |
| Day 3 | 4 | 22 |
| Erythremia | 2 | 11 |
| Respiratory distress | | |
| Labored respiration | 2 | 11 |
| Hyaline membrane disease | 0 | 0 |
| Congenital malformations | 4 | 22 |

approach has been to provide substrate (glucose) at a relatively high rate of delivery, as illustrated in Figure 6.

In conclusion, we believe that patient self-monitoring of blood glucose is a procedure that is relatively simple, practical, and acceptable to patients. It facilitates the attainment of glycemic control. It does require motivation, compliance with protocol, and an understanding of the overall approach to therapy. Yet it can be mastered by patients of all educational and socioeconomic levels. Although it is more costly than monitoring of urine, the improved glycemia that is attained has diminished our reliance on hospitalization during pregnancy, which eventuates in a savings of total costs for pregnancy management.

The need for meticulous attention to glycemic control during pregnancy mandates the frequent monitoring of glycemia. It is our opinion that this is best accomplished by patient self-monitoring on a daily basis. For patients with insulin-dependent diabetes, it would seem that such monitoring should now be a routine component of the treatment protocol.

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