The Infant of the Diabetic Mother

By RUPLA ESHAI, M.D., and RONALD L. GUTBERLET, M.D.

INTRODUCTION

Since Farquhar's description of the infant of a diabetic mother as being large, cushingoid, and plethoric and since the frequency of low blood sugars was described in the 1950s, much has been written about the management of pregnancy, labor, and delivery and the various problems of infants of diabetic mothers.

Perinatal problems have included stillbirth, large size for gestational age, hypoglycemia, hypocalcemia, hyperbilirubinemia, respiratory distress syndrome, polycythemia, heart failure, renal vein thrombosis, and congenital malformations. Recent additions have included subarachnoid hemorrhage, hyper- and hypokalemia, and adrenal crisis. These complications are seen both in infants of diabetic mothers (IDM) and in infants of gestational diabetic mothers (IGDM). As reported in 1969 by Warrner and Cornblath from a study made in 1966-68, the incidence of most complications is higher in the IDM.

There have been continued refinements in the monitoring of pregnancy with maternal urinary estriol determinations and oxytocin challenge tests to assess fetal well-being, amniotic fluid determination of the lecithin-sphingomyelin (L/S) ratio to predict fetal maturity, careful maternal diabetes control, and fetal monitoring during labor. Care of the sick newborn has likewise seen advances, including the use of continuous positive airway pressure in hyaline membrane disease, open radiant-heated beds, more universal use of intravenous fluids, and replacement transfusions.

The purpose of this article is to review the problems of IDM and IGDM and compare the incidences in infants born in 1971-73 with those in the previously mentioned study of Warrner and Cornblath (1966-68).

POPULATION

There were 6,493 infants delivered at the University of Maryland Hospital during 1971-73. Fifty-six infants were delivered to non-insulin-dependent and insulin-dependent diabetic mothers (nine per 1,000 births). There were incomplete data on four, and the remaining 52 form the basis of the information presented here. Maternal diabetes was classified on the basis of White's modified system. Thirty-three class A mothers had gestational diabetes and required only diet control. The 19 non-class A mothers were insulin-dependent.

Urinary estriol excretion was monitored in 16 mothers at first monthly, later weekly, and then daily. Since decreasing urinary estriols do not always correlate with fetal outcome, mothers at 34 weeks had oxytocin
challenge tests at three-to-seven-day intervals. Amniocenteses were done in nine mothers with decreasing urinary estriol excretion and/or positive oxytocin challenges to determine creatinine levels and I/S ratio. None of these nine required delivery before 37 weeks.

All infants were screened for hypoglycemia at two, four, six, 12, 24, and 48 hours. Chest x-ray, ECG, serum bilirubin, calcium, electrolytes, blood gases, hematocrits, cultures, and urinalysis were obtained as clinically indicated. Incidences were compared with the previous study (1966-68) and results analyzed by chi-square.

RESULTS

Two IGDM (6 per cent) and two IDM (10 per cent) were stillborn. The total is significantly higher than the 1.2 per cent stillbirth rate for the hospital during this period ($P<0.01$). Two of the mothers had no prenatal care. Comparisons between the 1971-73 and 1966-68 studies and between IDM and IGDM are given in the accompanying tables and figures. Of the 48 liveborn infants, the proportion of IDM to IGDM (17:31) was similar to that in 1966-68 (19:31).

Maternal age and parity were similar in all groups (Table 1). The overall number of abortions and stillbirths was similar in the two studies. Although the number of abortions in the insulin-dependent diabetic was greater in 1966-68, the difference is not significant ($P>0.05$). Mean gestation was one week earlier for both IDM and IGDM in 1971-73. Twenty-seven (87 per cent) IGDM and 12 (70 per cent) IDM were term.

Twelve (39 per cent) of the IGDM and 10 (59 per cent) of the IDM were delivered by cesarean section. Although the number of cesarean sections increased over those reported in 1969 (23 per cent of IGDM and 32 per cent of IDM), the difference is not statistically significant ($P>0.05$ and $>0.05$).

Race, sex, birth weight, and appropriateness for gestational age were similar in the two series (Table 2). The only exception was that the

### TABLE 1

**COMPARISON OF MATERNAL HISTORIES**

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<tbody>
<tr>
<td>Maternal age (yrs.)</td>
<td>Mean 25.16-37</td>
<td>Mean 28.17-44</td>
<td>Mean 29.17-43</td>
<td>Mean 27.16-44</td>
</tr>
<tr>
<td>Parity</td>
<td>2 1-7</td>
<td>2 1-7</td>
<td>3 1-7</td>
<td>3 1-10</td>
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<tr>
<td>Abortions</td>
<td>8 9.5%</td>
<td>16 21.9%</td>
<td>13 11%</td>
<td>10 7.7%</td>
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<tr>
<td>Stillbirths</td>
<td>2 2.4%</td>
<td>2 2.7%</td>
<td>2 1.4%</td>
<td>1 0.7%</td>
</tr>
<tr>
<td>Gestation (weeks)</td>
<td>38 36-40</td>
<td>37 36-40</td>
<td>39 34-42</td>
<td>38 30-41</td>
</tr>
<tr>
<td>Cesarean sections</td>
<td>10 58.9%</td>
<td>6 27%</td>
<td>12 38.7%</td>
<td>7 23%</td>
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### TABLE 2

**BIRTH CHARACTERISTICS**

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<tbody>
<tr>
<td>Total</td>
<td>17 100%</td>
<td>31 100%</td>
<td>31 100%</td>
<td>31 100%</td>
</tr>
<tr>
<td>Female</td>
<td>11 64%</td>
<td>11 36%</td>
<td>11 36%</td>
<td>11 36%</td>
</tr>
<tr>
<td>Black</td>
<td>12 69%</td>
<td>19 60%</td>
<td>19 60%</td>
<td>19 60%</td>
</tr>
<tr>
<td>SGA</td>
<td>0 0%</td>
<td>2 6%</td>
<td>2 6%</td>
<td>2 6%</td>
</tr>
<tr>
<td>LGA</td>
<td>10 59%</td>
<td>10 32%</td>
<td>10 32%</td>
<td>10 32%</td>
</tr>
<tr>
<td>Apgar ≤6 at 1 min.</td>
<td>4 13%</td>
<td>6 31%</td>
<td>6 31%</td>
<td>6 31%</td>
</tr>
<tr>
<td>Apgar ≤6 at 5 min.</td>
<td>0 0%</td>
<td>0 0%</td>
<td>0 0%</td>
<td>0 0%</td>
</tr>
</tbody>
</table>

Birth weight (gm. mean & range) 3,684 (2,580-3,068), 3,139 (1,021-3,463)

two small-for-gestational-age (SGA) infants in 1971-73 were IDM and the three SGAs in 1966-68 were IGDM.

Low one-minute Apgar score distributions were similar; however, low scores at five minutes occurred in four infants in 1966-68 and in none in 1971-73 ($P<0.05$).

**INFANT COMPLICATIONS**

**Hypoglycemia.** Cord serum glucose was obtained in 15 infants. In five of these, the glucose value was greater than 150 mg./100 ml. Two of these five and two of the 10 with cord glucose less than 150 mg./100 ml. developed hypoglycemia.

Serum glucose less than 30 mg./100 ml. was found in two IGDM (6.5 per cent) and five IDM (41 per cent). Serum glucose less than 20 mg./100 ml. occurred in two IGDM (6.5 per cent) compared with 16 per cent in 1966-68 ($P>0.05$) and three IDM (18 per cent) compared with 58 per cent in 1966-68 ($P<0.05$) (Figure 1).

All but one infant who became hypoglycemic in the study were so within the first three hours of life. The exception was diagnosed at 10 hours. Two infants had symptoms of hypoglycemia (jitteriness). All others were diagnosed by routine screening. Treatment of these infants has been outlined previously. All received 1 gm./kg. of 25 per cent glucose by intravenous infusion at 1 ml./kg./min., followed by a constant 10 to 15 per cent glucose infusion to maintain a serum glucose value over 30 mg./100 ml. Two infants had recurrences secondary to the abrupt discontinuation of 10 per cent glucose infusion. The recurrences were treated in a similar manner. No glucagon was used in this series.

**Hyperbilirubinemia.** Incidence of hyperbilirubinemia (serum bilirubin $>10$ mg./100 ml.) was similar in the two IGDM groups, but decreased from 63 per cent in 1966-68 to 18 per cent in 1971-73 in the IDM ($P<0.05$). The range of maximum bilirubin was 10 to 18 per cent. Five were treated with phototherapy and none required exchange transfusion, compared with two IDM in 1966-68 who did.

**Hypocalcemia.** Cord calcium levels were obtained in 11 infants, and all were within the normal range. Only infants clinically ill with other problems developed hypocalcemia.

**Respiratory distress syndrome.** Four IGDM (13 per cent) and one IDM (6 per cent) had some respiratory distress. Two had hyaline membrane disease, two transient tachypnea, and one type 2 respiratory distress syndrome. The overall incidence and severity were low and milder than in 1966-68, when 26 per cent of IDM had respiratory distress.

**Polycthemia.** On the first day of life, cord and/or central hematocrits were obtained in 27 infants (13 IDM and 14 IGDM) and gave values ranging from 41 to 73 per cent. A value greater than 64 per cent was found in only one IDM (7.7 per cent) and one IGDM (7.1 per cent) (Figure 2). Neither of the infants had symptoms related to cardiovascular system overload or congestive cardiac failure. In 1966-68, 30 per cent of IGDM and 42 per cent of the IDM had hematocrits greater than 64 per cent.

**Gastrointestinal abnormalities.** Two IGDM and one IDM had meconium plug syndrome. One of these, who had an umbilical artery catherization, subsequently developed pseudomomas peritonitis. Another had Hirschsprung's disease, and the third had no other associated pathology.

Another IDM developed necrotizing enterocolitis.

**Congenital malformations.** Three infants had congenital malformations.
One IGDM had a club foot; another had congenital heart disease. The third (IDM) is the above-mentioned infant with Hirschsprung's disease. This incidence is similar to that in 1966-68.

**Mortality.** No infants died in the new series, as compared with two IDM, one with hyaline membrane disease and the other with central nervous system malformation, in 1966-68.

**Other laboratory data.** Urinalysis was done in 13 infants (four IDM and nine IGDM). On initial examination, two IDM and one IGDM had microscopic hematuria, which cleared without therapy. Electrocardiograms were obtained in 11 infants. All but two gave normal results. One (in an IGDM) was interpreted as biventricular hypertrophy, the second as exaggerated right-axis deviation. In follow-up studies, results were normal for both.

Chest x-rays were obtained in 19 infants. The five abnormal results were in the five infants with respiratory distress syndrome. All findings were compatible with the clinical disease.

**DISCUSSION**

The infant of the diabetic mother continues to be at risk. The number of stillbirths remains high. Pregnancy monitoring might, however, have reduced the rate by half in this series if all mothers had sought prenatal care. That careful monitoring may reduce morbidity is supported by the fact that no infant in this series had a low Apgar score at five minutes.

Aside from differences between IDM and IGDM, there are differences between the two study periods with regard to hypoglycemia, hyperbilirubinemia, respiratory distress, and polycythemia in the IDM. Although the mean gestational age was one week later in 1971-73, there are continued
insufficient data to analyze the difference for significance.

The lower incidence of hypoglycemia in 1971-73 has several possible explanations. Better diabetic control during pregnancy could result in less hyperglycemia and less fetal hyperinsulinism. If the large size of the IDM reflects hyperinsulinism, however, one would have expected the incidence of hypoglycemia to be higher in 1971-73, since the incidence of LGA-IDM was higher than in 1966-68 (59 versus 36 per cent). Very early use of intravenous fluids may have had an effect. During 1971-73 all infants symptomatic at birth were immediately given an infusion of 10 per cent glucose via an umbilical artery or peripheral vein. Bolus infusions of glucose and bicarbonate were also given for metabolic acidosis. These therapies may lead to higher blood glucose levels\(^{12}\) and prevent hypoglycemia.\(^{13}\)

The lack of significant polycythemia in the current series is difficult to assess. Hematocrits were usually obtained from a central source. Hydration may play a role, especially in discordant values. No infant had renal vein thrombosis.

The lowered incidence of significant jaundice may be related to possible differences in the lack of both polycythemia and dehydration. In both series, gestational age was 36 weeks or more for all IDM. Photo-therapy may have prevented the jaundice from reaching exchange transfusion levels.

The differences in mean gestational age could explain the difference in incidence of respiratory distress. François et al.\(^{7}\) found that the incidence of hyaline membrane disease in IDM dropped from 15.4 per cent before 1971, when the mean gestational age was 36 weeks, to 8 per cent after 1971, when the mean gestational age was 37 weeks.

Two of the three infants with meconium plug syndrome had no known underlying gastrointestinal tract pathology. The relationship to the diabetes is not known.

CONCLUSIONS

The infant of the diabetic mother continues to be an at-risk perinate. Improvement in complication rates over the past decade may reflect better pregnancy monitoring, with delivery closer to term of less stressed infants. Continuing advances in neonatal care may also have contributed to this reduction in morbidity and mortality.

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**BIBLIOGRAPHY**