Neonatal Care of the Infant of the Diabetic Mother
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Objectives  After completing this article, readers should be able to:

1. Describe the most significant factor influencing neonatal morbidity in the diabetic pregnancy.
2. Characterize the impact of maintaining as normal a metabolic state as possible on the potential for perinatal and neonatal complications.
3. Describe the optimal location and services for delivery of a diabetic parturient.
4. Characterize the evaluation of an infant of a diabetic mother who requires resuscitation after birth.
5. Delineate the factor that most increases the chance of successful management of an infant of a diabetic mother in a regular nursery setting.

Introduction  Although many infants of diabetic mothers (IDMs) have an uneventful perinatal course, there is still an increased risk of complications, even in the infant born to the woman who has gestational diabetes. This discussion highlights specific factors that are critical in the immediate care of the IDM in the delivery room, in the nursery, and after discharge from the hospital. The care of this neonate builds on the pathophysiologic concepts presented in “The Infant of the Diabetic Mother” also appearing in this issue and other recent reviews of the subject. (1)(2)

Perinatal Mortality and Morbidity  The physician responsible for the care and delivery of the parturient must inform the neonatologist, pediatrician, or their designee responsible for the care of the neonate of the mother’s condition well in advance of delivery to ensure optimal care of the newborn. Among the specific factors that are of utmost importance are the type of diabetes and degree of maternal control, prior pregnancy history, and complications occurring during the pregnancy, including data about fetal monitoring for determination of fetal size and maturation. This information allows the physician caring for the neonate to anticipate many, if not most, of the potential fetal and neonatal complications and assist in determining if a neonatologist needs to be present at delivery.

It has been suggested for many years that the pregnant insulin-dependent diabetic woman can be managed at a hospital away from a centralized facility only if the hospital has an antenatal endocrine department and a neonatal special/intensive care unit. (3) However, not all pregnant diabetic women may be able to be transferred to a regional maternal and neonatal center. Thus, it is very important that the physicians caring for the mother and for the neonate anticipate potential complications.

Hanson et al (4) evaluated factors that influenced neonatal morbidity in the diabetic pregnancy. Among 92 consecutive pregnancies of White classes B through F, those associated with severe morbidities had longer durations of maternal diabetes, younger gestational age at birth, higher rates of cesarean section, and higher frequencies of toxemia. The most significant single factor was the gestational age of the pregnancy. Glucose control of 70 to 153 mg/dL (3.8 to 8.5 mmol/L) did not influence morbidity. Thus, as is well accepted, maintenance of as normal a metabolic state as possible, including
euglycemia, should diminish, but not completely eradicate, the increased perinatal and neonatal mortality and morbidities of the diabetic pregnancy.

Resuscitation
As with any neonate who is considered high risk, the IDM requiring resuscitation and stabilization immediately after delivery should be cared for in a designated resuscitation area. As noted in the Guidelines for Perinatal Care developed by the American Academy of Pediatrics and the American College of Obstetrics and Gynecology, (5) resuscitation should take place in a fully equipped area containing equipment required for skilled resuscitation. (A detailed description of the optimal facility can be obtained from the guidelines.) Specific personnel should be available, who can devote their complete attention to the neonate. The American Heart Association and the American Academy of Pediatrics have produced materials for teaching resuscitation skills. (6) All neonates should be dried initially to maintain as close to a neutral thermal environment as possible. Evaluation of the neonate in the resuscitation room requires observation for multiple factors (Table 1).

Macrosomia, Birth Injury, and Asphyxia
The neonate of the poorly controlled diabetic parturient often appears macrosomic (> 4 kg [8 lb 13 oz] or >90th percentile in weight for gestational age) compared with the neonate born to the woman who has well-controlled diabetes and or the woman is not diabetic or obese. (1) The consequence of undetected fetal macrosomia may be a difficult vaginal delivery due to shoulder dystocia, with resultant birth injury and or asphyxia. Other potential birth injuries are listed in Table 2.

Injury to the brachial plexus may have a variety of presentations because of damage to nerves of the brachial plexus. In addition to the obvious injury to nerves of the arm, diaphragmatic paralysis occurs if the phrenic nerve is affected. Because of associated organomegaly in the IDM, hemorrhage in the abdominal organs is possible, especially in the liver and adrenal glands. Hemorrhage in the external genitalia of the large neonate has also been observed.

Because the infant and his or her mother may be high risk, intrapartum monitoring is essential to minimize potential complications. At delivery, the nursing personnel evaluating the neonate should assign Apgar scores at 1 and 5 minutes to document the presence or absence of asphyxia. Although the specific cause of asphyxia is unclear, it may be caused by difficulty in the intrapartum period due to relative macrosomia. A cord pH can provide early biochemical assessment of the fetal physiologic status.

Asphyxia may have diverse consequences. It may affect respiratory, renal, central nervous system, and gastrointestinal functioning acutely. Decreased fluid intake may be indicated until the degree of injury to the kidneys and the central nervous system can be determined. An important complication of asphyxia in the neonate may be later respiratory distress.

Congenital Anomalies
Although most of the morbidity and mortality data for the IDM have shown improvement with advances in the care of the parturient during pregnancy, congenital anomalies (Table 3) remain a major unresolved problem.

Table 1. Observation of the IDM in the Resuscitation Room
- Asphyxia
- Birth injury
- Congenital malformations
- Evidence of macrosomia
- Hypoglycemia
- Respiratory distress

Table 2. Potential Birth Injuries in the IDM
- Abdominal organ injury
- Brachial plexus injury
- Cephalohematoma
- Clavicular fracture
- Diaphragmatic paralysis
- External genitalia hemorrhage
- Facial palsy
- Ocular hemorrhage
- Subdural hemorrhage

Table 3. Patterns of Congenital Malformations in the IDM
- Major congenital heart disease
- Musculoskeletal deformities, including caudal regression syndrome
- Central nervous system deformities (anencephaly, spina bifida, hydrocephalus)
The three- to four-fold increase in the incidence of congenital anomalies in the IDM is a frequent contributor to perinatal mortality. (7)

The pathogenesis of the increased frequency of congenital anomalies among the IDM remains obscure. (8) The critical period of teratogenesis occurs before the seventh week postconception.

Cardiomyopathy in the IDM can be congestive or hypertrophic. Hypertrophic cardiomyopathy in the neonate has been associated with poorly controlled diabetes in the mother and neonatal hypoglycemia. Respiratory distress can be accompanied by septal hypertrophy, (9) with resolution of symptoms within 2 to 4 weeks and of the hypertrophy within 2 to 12 months. (10) Hypertrophy of the interventricular septum and walls of the right and left ventricles also has been reported. (11) Profound hypoglycemia after birth, consistent with the metabolic effects of neonatal hyperinsulinism, has been strongly associated with septal hypertrophy. (12) Fetal hyperinsulinism may contribute directly to septal hypertrophy.

Although cardiac hypertrophy, apart from congenital heart disease, has been recognized in autopsies of IDMs for the past 3 decades, only within the last decade has attention been directed to a peculiar form of subaortic stenosis similar to the idiopathic hypertrophic subaortic stenosis found in adults. (13) This peculiar entity might be associated with symptomatic congestive heart failure. As with the adult variant, therapy with digoxin is contraindicated because the resultant increased myocardial contractility has been reported to be deleterious. Propranolol appears to be the therapeutic drug of choice. Clinically this disorder resolves spontaneously over a period of weeks to months, with accompanying correction of the echocardiographic features.

### Respiratory Distress

Respiratory distress, including respiratory distress syndrome (RDS), is a frequent and potentially severe complication in the IDM, although the trend toward delivering the diabetic patient later rather than earlier in gestation (assisted by improvements in the assessment of fetal well-being) is lowering the incidence. There also are other causes of respiratory distress in the IDM (Table 4). All of these conditions should be considered in the differential diagnosis of the neonate who has respiratory difficulty. Unfortunately, to date there have been no controlled trials of administration of exogenous surfactant to the IDM to determine if the response differs from that of the neonate who is not an IDM.

### Table 4. Causes of Respiratory Distress Other Than Respiratory Distress Syndrome in the IDM

- Cardiac disease
- Diaphragmatic paralysis
- Meconium aspiration
- Pneumomediastinum
- Pneumothorax
- Transient tachypnea

### Hypoglycemia

A rapid decline in plasma glucose concentration after delivery is characteristic of the IDM, especially one whose mother’s diabetes was poorly controlled. Values of less than 30 to 45 mg/dL (1.7 to 2.5 mmol/L) at term are abnormal and may occur within 30 minutes after clamping the umbilical vessels. Factors that influence the degree of hypoglycemia include previous maternal glucose homeostasis and maternal glycemia during delivery. (14) An pregnant woman whose diabetes is inadequately controlled would have stimulated the fetal pancreas to synthesize excessive insulin that may be readily released. Administration of intravenous dextrose during the intrapartum period that results in maternal hyperglycemia (glucose >125 mg/L [6.9 mmol/L]) will be reflected in the fetus and will exaggerate the neonate’s normal postdelivery decline in plasma glucose concentration. Hypoglycemia may persist for 48 hours or more or may develop after 24 hours.

The neonate exhibits transitional control of glucose metabolism, which suggests that a multiplicity of factors affect homeostasis. Many of the factors are similar to those that influence homeostasis in the adult. However, there is blunted splanchnic (hepatic) responsiveness to insulin in both the preterm and term neonate compared with the adult. (14) What have not been studied in the IDM are the many contrainsulin hormones that influence metabolism. If insulin is the primary glucoregulatory hormone, the contrainsulin hormones assist in maintaining a balance between insulin and other factors.

### Nursery Care

The presence of the specific morbidities discussed in this article requires specialized care by individuals who have the knowledge, training, and experience to handle subsequent care and follow-up. The clinician must decide whether to observe the IDM in a special care nursery or
in a regular nursery, assuming both exist in the hospital of
delivery, or to transfer the neonate to an intensive care unit
at a referral center. Reasons suggesting the need for
specialized care are listed in Table 5. Irrespective of
whether the neonate stays at the delivery hospital or is
transferred, specific metabolic abnormalities that should
be sought include hypoglycemia, hypocalcemia, hypomag-
nesemia, polycythemia, and hyperbilirubinemia.

**Glucose Homeostasis**

As noted, the IDM is a prime example of the potential for
glucose disequilibrium in the neonate. Because of the
transitional nature of glucose homeostasis in the new-
born period in general, accentuation of disequilibrium
may be enhanced in the IDM due to metabolic alter-
ations in the mother. Preventive therapy obviously in-
cludes rigid control of maternal blood glucose concen-
trations during the pregnancy and the perinatal period.

Blood for plasma glucose concentration should be
obtained at delivery from the umbilical cord. The IDM
can appear asymptomatic even with a relatively low
plasma glucose concentration. This may be due to the
initial brain stores of glycogen, although the exact bio-
chemistry is as yet undefined.

The use of various glucose strips and meters for de-
termining glucose concentrations has been called into
question. Theoretically, specific chemical determination
by a glucose analyzer is indicated, especially if a glucose
reflectance meter is used. Data suggest that glucose
reflectance meters probably should not be used with
capillary heel stick blood because results are less accurate
and reliable than when using blood obtained by a venous
stick. (15)(16)(17) If a meter or strip is used, results
should be confirmed by laboratory measurement.

The IDM may require parenteral treatment for main-
tenance of glucose homeostasis. Early administration of
oral feeding at fewer than 3 to 4 hours of age may be
beneficial to maintain plasma glucose concentrations that
are not in the hypoglycemic range.

The neonate who has a glucose concentration of less
than 30 mg/dL (1.7 mmol/L) should be treated with
intravenously administered glucose. Bolus injections
without subsequent infusion will only exaggerate the
hypoglycemia by a rebound mechanism and are contra-
indicated. Once the plasma glucose concentration stabi-
lates at greater than 45 mg/dL (2.5 mmol/L), the
infusion rate should be decreased slowly while oral feed-
ings are initiated or advanced. If symptomatic hypogly-
cemia persists, higher infusion rates of more than 8 to
12 mg/kg per minute may be indicated. Because most
neonates are asymptomatic, glucagon administration to
prevent hypoglycemia after delivery does not appear war-
ranted. Furthermore, glucagon may stimulate insulin
release that may exaggerate the tendency for hypoglyce-
mia.

Prompt recognition and treatment of hypoglycemia
has minimized sequelae. No specific late central nervous
system complications have been attributed to neonatal
hypoglycemia per se in the IDM.

Ultimately, the neonate requires full oral supplemen-
tation. Although proprietary formula is available, there is
no contraindication to breastfeeding by the mother who
is metabolically stable. A recent detailed review of the
treatment of hypoglycemia in the neonatal period pro-
vides for an attempt at early introduction of oral or
gavage feedings if the neonate is not symptomatic or has
a glucose concentration of more than 30 to 45 mg/dL
(1.7 to 2.5 mmol/L). (18) Table 6 lists an algorithm for
the treatment for symptomatic versus asymptomatic hy-
poglycemia, depending on the plasma glucose concen-
tration.

**Hypocalcemia and Hypomagnesemia**

Beyond hypoglycemia, hypocalcemia (calcium
<7 mg/dL [0.39 mmol/L]) ranks as one of the major
metabolic derangements observed in the IDM. (19)
Serum calcium is elevated after an increase in parathyroid
hormone (PTH) concentration.

Approximately 50% of the neonates born to women
who have type 1 diabetes develop hypocalcemia during
the first 3 days after birth. (19) Evaluation of the mech-
ani sm has failed to establish prematurity or asphyxia per
se as associated factors. However, the frequency and
severity of serum hypocalcemia is related directly to the
severity of the diabetic condition and is potentiated if
birth asphyxia is superimposed on the clinical condition.
It has been postulated that the mechanism that at least in
part is responsible for hypocalcemia is hyperphos-
phatemia that is apparent during the first 48 hours after birth.

Failure of an appropriate rise in PTH concentration in response to hypocalcemia has been reported in the IDM, in contrast to both infants of women who have gestational diabetes and nondiabetic women. The PTH response in the normal neonate that may occur on the second or third day after birth does not occur in the IDM until 48 hours or later on the third or fourth day. There is some evidence that maternal diabetes may be related to suppressed neonatal parathyroid function. (19)

Hypomagnesemia (magnesium $<1.5$ mg/dL [0.62 mmol/L]) has been found in as many as 33% of IDMs. As with hypocalcemia, the frequency and severity of clinical symptoms are correlated with the maternal diabetic status. Neonatal magnesium concentration has been correlated with the maternal diabetic status as well as with the maternal requirement for insulin and concentration of intravenous glucose administered to the neonate. (19) Hypocalcemia in the IDM may be due to decreased hypoparathyroid function resulting from the hypomagnesemia. Hypocalcemia and hypomagnesemia that have clinical manifestations similar to those of hypoglycemia must be considered and treated appropriately (Table 7). The long-term deleterious effects of both hypocalcemia and hypomagnesemia have not been documented.

Hyperbilirubinemia and Polycythemia

Hyperbilirubinemia is observed more frequently in the IDM than in the normal neonate. The pathogenesis remains uncertain. Prematurity (ie, biochemical immaturity) has been rejected as an explanation. (20)(21) Polycythemia is observed frequently in the IDM and may be the most important factor associated with hyperbilirubinemia. A venous hematocrit of at least 65% to 70% (0.65 to 0.70) has been observed in 20% to 40% of IDMs during the first few days after birth. Signs and symptoms may include jitteriness, seizures, tachypnea,
and oliguria. Therapy involving partial exchange transfusion of 10% to 15% of the total blood volume through the umbilical vein with normal saline or 5% albumin has been associated with a rapid resolution of symptoms in the symptomatic neonate.

**Long-Term Follow-Up**

What are the long-term effects of maternal diabetes on growth and development, psychological and intellectual capabilities, and the risk to the neonate of subsequently developing diabetes? What parameters of growth and development need to be followed into infancy and beyond?

An early prospective study of growth and development of the IDM suggested that excessive weight is almost 10 times more common in children of diabetic mothers than unusually low weight, which may represent a potential “return to obesity” noted at birth in this group of neonates. (22) A more recent study found that the neonate weighing more than 4 kg (8 lb, 13 oz) had significant elevations of height or weight at the time of entrance to school. (23) Vohr and associates (24) suggested that macrosomia in the IDM may be a predisposing factor for later obesity because at 7 years of age, 8 of 19 IDMs (42%) who had been large for gestational age at birth were obese compared with only 1 of 14 (7%) who had been appropriate for gestational age. When body weight and length and head circumference were evaluated from birth through 48 months of age, children of mothers who had poor glycemic control during pregnancy showed higher values for weight and weight-to-height ratio in infancy compared with neonates of well-controlled mothers. (25) Studies have shown that the offspring of a woman who has gestational diabetes is at increased risk for developing obesity during adolescence and glucose intolerance in young adulthood. (26)/(27)

The high frequency of congenital malformations in the IDM may be directly or indirectly associated with neuropsychological handicaps. The incidence of cerebral palsy and epilepsy is three to five times higher in the IDM compared with infants of nondiabetic mothers, but the rate of mental retardation does not differ. (28) When present, the difficulties are related to extremes of maternal age, severity of diabetes, low birthweight for gestational age, or complications during pregnancy. Psychological evaluations of children at 1, 3, and 5 years of age suggested that the IDM is more vulnerable to intellectual impairment, especially if the child was born small for gestational age or if the mother’s pregnancy was complicated by acetonuria. (29) These data were confirmed by others. (30) Data also suggested that neurobehavioral development at birth and during childhood may be adversely affected in the offspring of women who have gestational diabetes and whose blood glucose concentrations are less than optimally controlled during the pregnancy. (27)

The question of whether the IDM has an increased likelihood of developing diabetes is important. If one parent has type 1 diabetes mellitus, the risk for a child is in the range of 1% to 6%. (31)/(32) Although family aggregates do exist, transmitted both through and within generations, a simple mode of inheritance is inconsistent with the reported data. (33) Some have suggested that a polygenic multifactorial model best explains the reported observations. (32) In essence, the history of maternal diabetes should not be overlooked.

As the premier example of metabolic disturbance in pregnancy and in the neonatal period, it is obviously important for the IDM to be followed carefully after discharge from the special or intensive care nursery.

**References**


NeoReviews Quiz

6. The higher neonatal morbidity associated with diabetes mellitus during pregnancy results from several factors. Of the following, the most significant determinant of neonatal morbidity in diabetic pregnancies relative to pregnancies in healthy mothers is a:
   A. Greater frequency of toxemia.
   B. Higher rate of cesarean section.
   C. Longer duration of maternal diabetes.
   D. Poorer control of glucose during pregnancy.
   E. Younger gestational age at birth.

7. The treatment of hypoglycemia in an infant of a diabetic mother includes a bolus administration of glucose (200 mg/kg body weight) followed by a continuous glucose infusion. Of the following, the most appropriate glucose infusion rate (mg/kg per minute) for correction of hypoglycemia is:
   A. 6 to 8.
   B. 8 to 10.
   C. 10 to 12.
   D. 12 to 14.
   E. 14 to 16.

8. A newborn is delivered by cesarean section at an estimated gestational age of 37 weeks. The maternal history is significant for insulin-dependent diabetes mellitus, fetal macrosomia, and failure to progress following spontaneous labor. The infant has evidence of respiratory distress. Of the following, the most likely cause of respiratory distress in this infant is:
   A. Diaphragmatic hernia.
   B. Hypertrophic cardiomyopathy.
   C. Meconium aspiration.
   D. Pneumothorax.
   E. Respiratory distress syndrome.
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