

# Modern Management of Diabetic Pregnancies\*

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On a broad national basis, it should be quite possible to substantially reduce maternal morbidity and the disproportionately high numbers of perinatal losses associated with diabetic pregnancies. Nationwide, the overall perinatal mortality rate for this group is approximately 20%, which is at least double that incurred in centers where intensive care facilities and personnel are available, and consistent, well-coordinated care by the health team is provided.

Although the prognosis for fetal survival is less favorable with advances in severity of the diabetic state, there is a significant risk even during the mildest stage of the disease. Careful prospective studies, notably those of O'Sullivan and his group, have demonstrated that gestational diabetics have a higher than normal perinatal mortality. Prevention begins with diagnosis.

**Detection.** Ideally, a two-hour postprandial screening of blood sugar following a 100 g carbohydrate-equivalent breakfast should be a standard prenatal laboratory test. In practicality, all patients with a poor obstetric history, previous perinatal losses, large babies, a family history of diabetes, glycosuria, or significant obesity are candidates for a glucose tolerance test. Using these criteria, we subjected 3,340 prenatal patients to the three-hour glucose tolerance test following a 100 g glucose load, and 540 showed abnormal responses. The yield of positives, therefore, was 1 in 6.3 suspects, and the overall incidence of gestational diabetes in this Philadelphia population was 1.18%. Criteria used are as follows: fasting = 90 mg %; 1 hour = 165 mg

%; 2 hour = 145 mg %; 3 hour = 125 mg %. Glucose tolerance is impaired if two or more of these values are equaled or exceeded. The test is performed on whole blood using the Somogyi method or autoanalyzer (Hoffman) method. If plasma or serum is used, 10 mg % should be added to each of the values. The importance of a very large screening program was shown in the prospective study conducted by O'Sullivan and his group who found that screening is particularly important in the obese, older-age patient. Perinatal mortality was 1.5% for normal control patients and 6.4% for those with gestational diabetes. The increase in perinatal loss was strikingly evident in gestational diabetic mothers 25 years of age or older, with the risk further increased by obesity.

**Metabolic Control.** How strict should this be? These patients are ketosis prone. Ketosis is one of the most lethal events for the fetus, but one of the most preventable complications for the mother. The incidence of intrauterine fetal death is greatly increased in pregnancies complicated by pre-coma maternal acidosis. Of further concern is the fact that the National Collaborative Study reveals a significant relationship between maternal ketonuria and central nervous system defects or deficiencies in the offspring. Neither insulin treatment nor hypoglycemia shows a positive association. For these reasons the patient should be kept as nearly normoglycemic as possible and free of ketonuria even at the expense of an occasional episode of hypoglycemia which is readily controlled.

Many, but not all, gestational diabetics can be maintained on diet alone. The response to diet is determined on the basis of a two-hour postprandial blood sugar obtained at two-week intervals. If the

\* The following summarizes the main points of a lecture presented by Dr. Carrington at the 46th Annual McGuire Lecture Series, December 5, 1974, at the Medical College of Virginia, Richmond.

two-hour value on diet cannot be maintained below 160 mg %, the patient needs insulin, and for the purpose of management of the pregnancy such patients should be considered in the insulin-dependent category.

Is there any advantage in treating all gestational diabetics with low-dose insulin? Several groups in this country and abroad have compared treated and untreated cases. Apart from slight reduction in oversized infants, other advantages are not yet sufficiently clear-cut to warrant recommending this approach. Oral hypoglycemic agents should not be used in pregnancy. In contrast to insulin, the sulfonyl ureas pass the placental barrier readily. Neonatal hepatic function is relatively immature, and the newborn metabolizes these drugs poorly. Intractable hypoglycemia persisting as long as the eleventh day of life, and in some instances requiring exchange transfusion, have been reported, particularly in relation to long-acting preparations such as chlorpropamide. The biguanides which raise the blood lactate level may accentuate the tendency to maternal ketoacidosis and are contraindicated during pregnancy.

The anti-insulin effects of pregnancy usually cause significant changes in insulin needs after the 20th week of gestation. The rise in requirement is sometimes precipitous about the 24th to 26th week. Both the patient and the physician should be on the lookout for these changes. In our patients, 75% needed a mean of about 60% more insulin. Twenty-three percent showed only minor increase in insulin requirement. Only an occasional patient showed reduction in insulin need.

One of the poorly understood problems has to do with remission, which may occur particularly in the early stages of diabetes. How does one handle the patient who states that she had an abnormal glucose tolerance test with her previous pregnancy and was treated accordingly, but the glucose tolerance test in the present pregnancy is normal? While it is the rule that the diabetic state will progress, remissions do occur. We have encountered this phenomenon in a number of gestational diabetics and in one case of juvenile diabetes. Since the adverse effect upon the fetus can occur at any stage including the prediabetic period, it is important to accept the reality of remission and to avoid the temptation to ascribe its occurrence to faulty initial diagnosis.

Most diabetics have some degree of hydramnios, excessive in approximately 10% of cases. The com-

mon practice of prophylactic use of diuretic and rigid salt restriction may do more harm than good. Thiazides are useful only in otherwise uncomplicated fluid retention. If administered alternately three days on and three days off, these drugs will often reverse simple fluid shifts without disturbing electrolyte balance, but they are ineffectual for reversal of toxemia or hydramnios. Hospitalization is necessary if these conditions develop. Asymptomatic bacteriuria is found in about 12 or 13% of diabetic pregnancies, or approximately twice the overall incidence, and should be treated when found.

**Prenatal Monitoring.** The ability to predict intrauterine fetal deaths in diabetic pregnancies on clinical evidence alone has limitations. A reliable method for assessing intrauterine fetal welfare should be available in every diabetic pregnancy. Although no single test is capable of detecting all types of malfunctions that affect the fetus, the urine estriol test is, in our experience, indispensable. The fact that estriol production requires a fetal as well as a placental component is an obvious advantage. The types of cases in which estriol values may be misleading are small in number and can usually be readily identified. These are mainly cases in which renal function is markedly reduced and renal clearance of estriol diminished.

Although the majority of patients with mild diabetes can be maintained free of complications and await labor at term, some cannot. Fetal deaths do occur in the virtually asymptomatic, well-controlled gestational diabetic pregnancy. In these cases, estriol determinations have proved to be of great value in identifying the fetus in jeopardy who should be delivered and, on the other hand, in providing reassurance and safe conduct through the natural course of pregnancy when estriol values remain in the normal range.

Recent recommendations have been made to apply the same principles to pregnancies complicated by overt diabetes. While it is feasible to individualize and extend the timing of delivery to the 38th week or even beyond in many cases of B and C insulin-dependent diabetics, those with advanced disease are poor candidates for this approach, even with frequent monitoring. From a practical point of view, and purely on clinical grounds, pregnancy in a patient with angiopathy, retinopathy, or nephropathy can rarely be carried beyond the 37th week, and all too often the pregnancy has to be terminated before that

optimal time in the interest of the mother or baby or both. The suddenness with which serious changes or events can take place in these patients and the fact that methods for determining fetal maturity are available (particularly the lecithin/sphingomyelin ratio and the creatinine concentration) offset the possible advantages of attempting to extend the gestational period for Classes D, E, and F diabetics beyond 37 weeks.

The infant of a diabetic mother is at risk from the moment of birth. Respiratory distress is the greatest threat. It is most directly related to prematurity and accentuated in diabetes. While tests for fetal maturity should make iatrogenic prematurity preventable, early delivery will continue to be necessary in selected cases to avoid intrauterine fetal death or damage. The neonatologist experienced in dealing with respiratory pathophysiology who can

initiate treatment within minutes after birth, and a neonatal intensive care unit capable of providing clinical and laboratory support services on a 24-hour-a-day basis offer the best chance for intact survival.

In principle, the problems of diabetic pregnancies do not differ from the problems of at least two-thirds of all high-risk pregnancies, and in this respect, they serve as a prototype for centralized perinatal care. The demands in terms of medical and paramedical manpower, the high cost of services and facilities comprising the perinatal center, and the concern for quality of life will surely require revision of the current health care delivery system. Consolidation of scarce resources in centers, whether teaching or community hospitals, capable of providing specialized care for the high-risk mother and newborn is the logical approach.