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EDITORIAL

INFANTS OF DIABETIC MOTHERS

Management of the newborn infant of the diabetic mother is still one of the most challenging unsolved problems in clinical medicine. In spite of extensive investigations of the physiologic and biochemical status of the infant,[1-4] approximately 35 per cent die either in utero or in the neonatal period. Prematurity and anomaly are increased in prevalence, albeit to what degree has not been established. The infants behave in many respects like premature infants even though they often are large and appear postmature. The most common cause of death in the neonatal period is hyaline membrane disease.

It is now realized that increase in fetal survival has been achieved by reduction of stillbirth rather than of neonatal death.[1] The most successful results have been reported from centers where therapy is characterized by collaboration between diabetician, obstetrician, and pediatrician. Factors related to unsatisfactory outcome have been: long duration of known diabetes, complicating vascular disease, and uncontrolled diabetes. Although it is generally held that early interruption of pregnancy will reduce the occurrence of stillbirth, conclusive evidence of this is not yet available. Good diabetic control is very important, a view which we base on long-term observation of a large group of juvenile diabetic pregnancies at the University of Iowa.

Fetal loss is also increased in patients destined to develop chemical diabetes in later years.[5] Unfortunately, neither prediabetes or mild gestational diabetes may be suspected, and consequent lack of appropriate management may account in part for the fetal loss. In both these patients and those with established diabetes there has been no significant reduction in mortality beyond that made possible by improved care of the mother.

Very little is known about the physiology of the placenta in diabetic pregnancy. There is evidence that the organ remains immature. Of particular interest are the recent reports of Joron et al.[6] and Kyle.[7] These investigators studied maternal urinary estriol excretion during pregnancy and found it below that of nondiabetic pregnancies. Moreover, rapidly decreasing urinary estriol values indicated fetal distress. In fact, when levels fell to 4 mg./24 hrs. for forty-eight hours, fetal death had occurred.[7] Another significant study recently is that from Daughaday's laboratory.[8] Herein a growth hormone-like substance, probably placental in origin, was found in elevated concentration in diabetic pregnancy. The physiology of this substance remains to be determined, however.

At present much attention is being directed to the side effects of drugs on pregnancy. Of particular interest in the management of diabetic pregnancy are the chlorthiazides and the sulfonylureas. The former have been used liberally in the pregnant diabetic without deleterious effect reported so far. Though they create antagonism to insulin action, it has been difficult to separate a rise in insulin requirement brought on by chlorthiazides from that usually occurring as pregnancy progresses.[9] The latter compounds, the sulfonylureas, have not been recommended in gestational diabetes because of scattered reports of fetal abnormalities in pregnancies wherein these drugs were employed. No proof of a cause

and effect relation in animals or humans has been demonstrated, however.[10,11] Except for the sulfonylureas, no other drugs have been proposed so far as influential in development of the abnormalities of diabetic pregnancy.

Studies of the chemistry and physiology of infants of diabetic mothers have been numerous. In a number of centers, investigations of body composition have revealed the body weight to be increased because of fat rather than edema.[12-14] There is also excessive glycogen deposition. Cardiomegaly which is unrelated to the presence of glycogen may be encountered. Brains of the infants have been found to be small in relation to body weight.

Other studies have indicated a high level of plasma immunoreactive insulin at birth.[15] Increased circulatory insulin may contribute in part to the hypoglycemia occurring the first twenty-four hours of life. Such hypoglycemia may contribute to morbidity and eventual central nervous system damage if it is not promptly recognized and treated. It has been our practice to observe all infants of diabetic mothers closely for hypoglycemia during the first day of life.

Craig observed tetany in ten of fifteen infants of diabetic and prediabetic mothers.[16] All had serum calcium levels below 7 mg. per cent. The concentrations of blood glucose and urea nitrogen were normal, and none of the infants was premature by weight. Two instances of idiopathic hypoparathyroidism have been reported in infants of diabetic mothers.[17] Hyperbilirubinemia has been observed consistently.[18] It is not certain if there is change in 17-hydroxycorticosteroid production, though recent studies of Smith et al. indicate increase in the presence of the respiratory distress syndrome.[19-21]

Investigations of the development of respiratory distress have been few and inconclusive. In studies at our institution infants who did not develop hyaline membrane disease had blood volumes of 12-15 per cent and serum protein concentrations greater than 5.0 gm./100 ml. In contrast, some full-term infants who developed respiratory distress had markedly decreased blood volumes.[22] Information concerning blood volumes of infants of diabetic mothers during this period of distress is not yet available.

The management of pregnancy in diabetes requires the combined efforts of an internist, two obstetricians, an anesthesiologist, and a pediatrician. It is generally believed that delivery should be made not earlier than the thirty-fifth week, and preferably near the thirty-seventh week.[1] A trial of labor is desirable, followed by cesarean section when the labor is unsuccessful. It is advisable to employ short acting insulin and intravenous glucose on the day of delivery because of the marked drop in insulin requirement following delivery.

Following delivery, the infant should be managed as premature even though his weight be excessive. The importance of constant observation cannot be overemphasized, and unnecessary treatment and manipulation must be scrupulously avoided. The infant should be placed in a warm environment, preferably in an isolette for observation, and body temperature maintained as close as possible to 98.6° F. High concentrations of mist and humidity are probably unnecessary. We examine all infants for congenital anomalies immediately after birth. Observation is made for abdominal convexity, a rectal catheter is inserted, and gastric contents are aspirated. If there is evidence of central nervous system irritability such as excessive crying, reflex activity or twitching, serum calcium and glucose determinations are made, and calcium gluconate (1 ml.) and 50 per cent glucose (3 ml.) given promptly intravenously. Glucagon, 300 μg./kg. may be used on an emergency basis to correct hypoglycemia, although 50 per cent glucose is preferred. If early or pronounced icterus develops, 10 per cent glucose should be given orally or intravenously (60 ml./kg.) during the first seventy-two hours. We have not found it necessary to perform exchange transfusions except on rare occasions. If the infant does not develop distress, he is fed when he is active, appears hungry and begins to void frequently. This approach is believed to be more physiological than feeding at a specific age.

It is doubtful if any of the foregoing measures has significantly altered neonatal morbidity or mortality. Nevertheless, early and optimal therapy should be helpful in decreasing the occurrence of central nervous system damage. Little can be said concerning the therapy of hyaline membrane disease other than to recommend placement of the infant in a warm environment with sufficient oxygen to prevent cyanosis. Measures beyond this remain largely on an investigational basis.

In conclusion, it is clear that despite many investigations, almost nothing is known about the pathogenesis of abnormalities in diabetic pregnancy. The maternal factors which appear to have the greatest influence on outcome are severity, duration, and degree of control of diabetes. Age, parity, obstetric history, and insulin need of the mother, toxemia, and hydramnios have less effect.[2] The yield of live infants has increased, but only because of better supportive care of the mother and

child. It is hoped that new light will be shown on the cause and management of the abnormalities in the near future. In the meantime, the physician caring for the child must concern himself with improving the management of prematurity and hyaline membrane disease.

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