

## ABSTRACT SERVICE

### Diabetes and pregnancy

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*Normal pregnancy profoundly affects every aspect of intermediary metabolism. Pregnancy, the only truly physiological challenge to insulinogenic reserve, is accompanied by metabolic realignments designed to adapt the mother, (an intermittently feeding host) to a continuously feeding conceptus. The endocrine function of the conceptus and its effect on maternal fuels are responsible for the diabetogenic challenges of normal pregnancy. Pregnancy may be attended by "onset or first recognition" of carbohydrate intolerance (gestational diabetes mellitus) and insulin requirements may markedly increase in a previously detected diabetic (pregestational diabetes mellitus).*

*Pregnancy not only affects metabolism in the diabetic mother, it also influences foetal outcome. Perinatal losses in pregnancies complicated by diabetes remain disturbingly high in areas where poor socioeconomic conditions preclude access to medical facilities. Improved maternal and fetal surveillance in developed areas have substantially reduced perinatal losses. Indeed a number of centres report values, which approximate that found in general population. Foetal macrosomia and birth trauma, congenital anomalies and neonatal complications account for much of the foetal morbidity and mortality. Intensive efforts at screening high-risk women, frequent evaluations of identified women, meticulous glycemic control starting periconceptually and continuing throughout pregnancy, regular non-invasive assessment of fetoplacental integrity, delivery at term or near term and availability of neonatal intensive care unit are key management strategies.*

*Interest has been aroused in the concept of "fuel-mediated teratogenesis" with long-term effects on anthropometry, behaviour and organogenesis of infants of diabetic mother. Some important abstracts from literature are presented below.*

#### DIAGNOSIS

**Neely RDG, Kiwanuka JB, Hadden DR.**

**Influence of sample type on the interpretation of the oral glucose tolerance test for gestational diabetes mellitus.**  
**Diabetic Med. 1991;8:129-134.**

The World Health Organization (1985) criteria allow evaluation of the oral glucose tolerance test using venous or capillary whole blood or plasma glucose measurements. However, the empirical factors used for interconversion may not reflect observed differences, especially during pregnancy, causing inconsistent classification. To investigate how choice of sample would influence the interpretation of results, venous and capillary blood was taken during oral glucose tolerance tests in 36 pregnant women at risk of gestational diabetes and in 21 non-pregnant control subjects. Glucose was measured on whole blood and plasma by a glucose oxidase method. No cases of gestational diabetes were identified. Eight subjects had gestational Impaired Glucose Tolerance using either venous plasma or venous whole blood results, but only five were similarly classified with capillary whole blood and only four using capillary plasma. Plasma-whole blood differences (venous  $0.6 \pm 0.2$  ( $\pm$  SD) mmol/l, capillary  $0.7 \pm 0.3$  mmol/l) and capillary-venous differences (plasma  $0.5 \pm 0.4$ , whole blood  $0.4 \pm 0.5$  mmol/l) at 2 h were lower (all  $P < 0.05$ ) than in the WHO criteria  $1.1$  mmol/l). When compared with venous plasma, capillary measurements may give a lower incidence and venous whole blood measurements a higher incidence of Impaired Glucose Tolerance in pregnancy.

**Nasrat HA, Sabbagh SA, Saleh M, Ardawi M.**  
**New criteria for interpretation of the 75g, oral glucose tolerance test in pregnancy.**  
**Metab Clin Exp. 1990;39:51-7.** (From: Dept. of Obstetrics and Gynaecology, King Abdulaziz University Hospital, Jeddah, Saudi Arabia).

A 75g oral glucose tolerance test (OGTT) was performed on 135 high-risk pregnant patients. When the current World Health Organization (WHO) criteria for the diagnosis of gestational-glucose tolerance were applied, 88 patients were considered normal, 11 had gestational diabetes, and 36 patients had impaired-glucose tolerance, respectively. Plasma glucose, insulin, and C-peptide levels during the OGTT were further studied in the 88 patients (who had normal results). Two metabolically distinct groups were identified; a group ( $n=53$ ) with a 2 hour plasma glucose  $<6.6$  mmol/l ( $118.8$ mg/dl), had a normal insulin and C-peptide pattern, and a second group ( $n=35$ ) who had 2 hour plasma glucose  $>6.6$  mmol/l displayed a glycemic, insulin, and C-peptide pattern similar to that of patients with gestational diabetes mellitus. The risks of macrosomic babies and operative delivery were significantly greater in the latter group. These results suggest that in a pregnant population, a group of patients with impaired glucose tolerance will be underdiagnosed using the current WHO criteria. Based on these results new criteria for gestational glucose intolerance are suggested.

*Development of precise criteria can lead to consensus on the biological definition of gestational diabetes mellitus.*

#### PREVALENCE

**Buschard K, Hougaard P, Molsted-Pederson L, Kuehl C.**  
**Type 1 (insulin dependent) diabetes mellitus diagnosed during pregnancy: a clinical and prognostic study.**  
**Diabetologia 1990; 33: 31-5.**

The study concerns the clinical outcome and later prognosis (regarding permanent insulin treatment) of patients who develop insulin dependent diabetes mellitus during pregnancy (which is different from gestational diabetes). Sixty-three such patients ( $27 \pm 1$  (SEM) years old) were delivered at the Copenhagen Center for Diabetes and pregnancy during the years 1966-1980. Obstetric complications such as toxemia were seen in 9.5% of these study patients and the perinatal mortality was 6.3% both percentages being higher than in the general population (1.1%,  $p < 10^{-7}$  and 1.0%,  $p < 0.001$ ), respectively), but similar to those observed in patients with type-I diabetes diagnosed before pregnancy. In contrast, the frequency of malformations was 1.6%, the same as in the general population (1.4%), but lower than that seen in patients with long standing diabetes (8.3%,  $p < 0.05$ ). At follow-up examination  $8 \pm 1$  years after diagnosis all patients were diabetic; 77% were insulin treated, having no or virtually no residual beta-cell function, and were clearly type-I diabetic patients. After delivery 80% of the patients had a remission period (median 256 days) without insulin treatment. This remission period was absent or shortest in patients with following characteristic ( $p \pm 0.03$ ): low age, first parity, not overweight, and high blood glucose level at diagnosis. These prognostic parameters should be considered in obligatory clinical follow-up plans for such patients.

*Honeymoon after delivery.*

#### MATERNAL METABOLISM

**Buchanan TA, Metzger BE, Fienkel N.**  
**Accelerated starvation in late pregnancy: a comparison between obese women with and without gestational diabetes mellitus.**  
**Am. J. Obstet. Gynecol. 1990; 162:1015-20.**

The authors compared the glucose, insulin, free fatty acid and 3-hydroxybutyrate responses to a briefly extended overnight fast during the third trimester of pregnancy between 2 groups: obese women with normal glucose tolerance (n=10) and age and weight matched women with gestational diabetes mellitus (n=10). After a 12-hour overnight fast, plasma glucose ( $95 \pm 4$  mg/dl vs.  $78 \pm 2$  mg/dl;  $p < 0.01$ ), insulin ( $32 \pm 5$  uU/ml vs.  $17 \pm 2$  uU/ml;  $p < 0.02$ ), and free fatty acid ( $860 \pm 63$  mmol/l vs.  $639 \pm 79$  mmol/l;  $p < 0.05$ ) levels were higher in the patients with gestational diabetes mellitus. 3-Hydroxybutyrate levels were similar in the 2 groups at that time ( $0.23 \pm 0.04$  mmol/l vs.  $0.18 \pm 0.03$  mmol/l;  $p > 0.3$ ). When the fast was extended to 18 hours by having the patients skip breakfast, glucose levels fell more rapidly in the group with gestational diabetes mellitus but remained elevated compared with the non-diabetic women. Insulin levels declined at a similar rate in the 2 groups. Free fatty acid levels did not increase significantly in the group with gestational diabetes mellitus during the extended fast. In contrast, free fatty acid levels increased by 44% in the normal pregnant women, reaching the level observed in the group with gestational diabetes mellitus after 18 hours. 3-Hydroxybutyrate levels remained virtually identical in the 2 groups throughout the brief fast. Thus, compared with that of normal pregnant women, the response of obese women with gestational diabetes mellitus to brief caloric deprivation during late pregnancy was characterized by a greater fall in plasma glucose values without a greater propensity to ketosis. These findings may have important implications for the dietary management of obese patients with gestational diabetes mellitus.

*The common clinical practice of "skipping breakfast" for laboratory tests or other clinical procedures may not be without meaningful metabolic consequences in late pregnancy.*

**Bachanan TA, Metzger BE, Fienkel N, Bergmen RN.**  
**Insulin sensitivity and B-cell responsiveness to glucose during late pregnancy in lean and moderately obese women with normal glucose tolerance or mild gestational diabetes.**  
*Am. J. Obstet. Gynecol. 1990;162:1008-14.*

The authors used the minimal model technique to obtain concurrent measurements of whole-body insulin sensitivity and pancreatic B-cell responsiveness to glucose during the third trimester of pregnancy. Insulin sensitivity in normal pregnant women (n=8) was reduced to only 1/3 that of a group of non-pregnant women (n=7) of similar age and relative weight. This marked insulin resistance was compensated by reciprocal enhancement of the first and second phase insulin responses to intravenous glucose, which were increased threefold as compared with the non-pregnant women. Women with gestational diabetes mellitus (n=16) had mean insulin sensitivity similar to that of the normal pregnant group, which indicates that insulin action was appropriate for the late phase of pregnancy in the gestational diabetic group. By contrast, the mean first phase insulin response was significantly reduced in women with gestational diabetes mellitus, as compared with that of normal pregnant women ( $p < 0.001$ ). However, approximately 1/5 of the group with gestational diabetes mellitus had first phase responses that did not fall below the 95% confidence interval for the mean in normal pregnant women. The mean second phase response was also lower in the group with gestational diabetes, although the difference was of borderline statistical significance ( $p < 0.09$ ). These findings reveal the quantitative nature of the reciprocal changes in insulin sensitivity and beta-cell function that normally accompany late pregnancy. They further indicate that during the third trimester, mild gestational diabetes is characterized by an impairment of pancreatic beta-cell function rather than an exaggeration of the normal insulin resistance of late pregnancy.

**DIABETIC COMPLICATIONS**  
**Winocour PH, Taylor RJ.**

**Early alterations of renal functions in insulin dependent diabetic pregnancies and their importance in predicting pre-eclamptic toxemia.**

*Diabetes Res. 1989;10:159-64.*

Renal function, blood pressure and glycemic control were assessed during gestation in 23 non-azotemic insulin-dependent diabetic women. Pre-eclamptic toxemia (PET) developed in 9 cases, and was predicted by higher levels of albuminuria excretion, mean blood pressure and serum urate early in pregnancy, as well as by the primigravid state. Mean blood pressure, serum creatinine and urate remained stable in the first trimester and rose thereafter in women who developed PET. Levels of mean blood pressure were significantly higher in the second ( $p < 0.005$ ) and third ( $p < 0.0001$ ) trimesters, serum urate was higher in the first, second ( $p < 0.04$ ) and third ( $p < 0.001$ ) trimesters, as was AER ( $p$  range 0.02-0.0001), and serum creatinine levels were higher in the third trimester ( $p < 0.02$ ) in comparison to those women who did not develop PET. Glycemic control was similar in both groups. In addition, physiological alterations in creatinine clearance, and in serum levels of creatinine and urate were attenuated in cases uncomplicated by PET. Insulin-dependent diabetic pregnancies are characterized by disturbance of renal function early in pregnancy which may be predictive of PET, particularly in primigravidae and/or when accompanied by increases in mean blood pressure.

*Pregnancies in women with nephropathy are attended by higher incidence of pre-eclamptic toxemia, premature delivery and substantial greater neonatal morbidity.*

**Reece EA, Winn HN, Hayslett JP, Coulehan J, Wan M, Hobbins JC.**

**Does pregnancy alter the rate of progression of diabetic nephropathy?**

*Am. J. Perinatol 1990;7:193-7.*

The effect of gestation on the rate of decline of renal function was studied in 11 pregnancies complicated by diabetic nephropathy. For each pregnancy, serum creatinine levels were available within 4 years before pregnancy, during pregnancy, and within 4 years after delivery. Although all of these patients were hypertensive and had increased proteinuria during pregnancy, the mean serum creatinine just prior to conception ( $1.3 \pm 0.5$  mg/dl) and the last follow-up value ( $1.2 \pm 0.3$  mg/dl) were not significantly different. When the inverse of serum creatinine (1/Scr) was used to estimate creatinine clearance, the renal function was either improved or remained stable in the majority of the pregnancies (7/11). The observed decline in renal function through the end follow-up appeared to be consistent with the expected natural course of diabetic nephropathy in the absence of pregnancy. Furthermore, the slope for inverse serum creatinine before and after pregnancy was not significantly different. In conclusion, pregnancy in patients with mild to moderate diabetic nephropathy does not seem to accelerate the rate of decline in renal function.

*The study supports available data that mild to moderate diabetic nephropathy is not a contraindication for pregnancy. In spite of low number of published cases, a pregnancy may be successful in a diabetic woman after renal transplantation or even after renal and pancreatic transplantation.*

**Klein BE, Moss SE, Klein R.**

**Effect of pregnancy on progression of diabetic retinopathy.**

*Diabetes Care 1990; 13: 34-40.*

A prospective study was undertaken to determine the effect of pregnancy on diabetic retinopathy. Diabetic women on insulin therapy were enrolled; 1 group comprised of pregnant women, the other group comprised of women who were not pregnant. Women were evaluated on referral and again in the postpartum period. The severity of diabetic retinopathy was

based on grading of fundus photographs of 7 standard photographic fields. The glycosylated hemoglobin, duration of diabetes, current age, diastolic blood pressure, number of past pregnancies, and current pregnancy status were evaluated as risk factors for progression of diabetic retinopathy. After adjusting for glycosylated hemoglobin, current pregnancy was significantly associated with progression ( $p < 0.005$ , adjusted odds ratio 2.3). Diastolic blood pressure had a lesser effect on the probability of progression. The findings from this study indicate that pregnancy and level of glycemia are associated with progression of diabetic retinopathy.

*Other studies have shown that serious alterations in retinal status rarely occur during gestation in women with proliferative retinopathy who have been treated with photocoagulation. Thus it is prudent to assess retinal status carefully prior to pregnancy and delay conception till the retinal pathology has been stabilised.*

## **MANAGEMENT**

**Lean ME, Pearson DW, Sutherland HW.**

**Insulin management during labour and delivery in mothers with diabetes.**

**Diabetic Med. 1990;17:162-4.**

A standardized intravenous regimen has been assessed, in 25 insulin treated diabetic women, for insulin and dextrose therapy in labour and delivery. Adjustments to insulin infusion rate are determined by trends in blood glucose as well as by absolute concentration, in order to approach normoglycemia. Blood glucose was 5.0 (SD 1.7) mmol/l on arrival in labour (or at 0800 h before planned delivery) and was maintained at 6.0 (SD 1.8) mmol/l with insulin 0.5 U/h for up to 29 h before delivery, when it was 6.3 (SD 2.1, range 3.0-9.0) mmol/l with insulin infusion rate 0-4 U/h. Neonatal blood glucose ( $< 2.0$  mmol/l in 11 babies) correlated with both maternal HbA ( $r_s = 0.47$ ,  $p < 0.02$ ) and maternal blood glucose at delivery ( $r_s = 0.58$ ,  $p < 0.01$ ). During 12 months observation on the intravenous regimen, 339 measurements of blood glucose were made; 10 were  $< 3.0$  mmol/l, 242 were 3.0-8.0 mmol/l, and 81 were  $> 8.0$  mmol/l (mean 6.5, range 2.7-13.5 mmol/l). Insulin infusion rate range from 0 to 5 U/h, with 139 rate adjustments. Only 1 mid clinical hypoglycemic episode, responding to increased dextrose infusion, was recorded. This simple flexible regimen proved clinically reliable for both midwifery and medical staff.

## **FETAL OUTCOME**

**Forsbach G, Contreras-Soto JJ, Fong G, Flores G, Moreno O.**

**Prevalence of gestational diabetes and macrosomic newborns in a Mexican population.**

**Diabetes Care 1988;11: 235-238.**

Prevalence of gestational diabetes was investigated in 693 pregnant patients between the 24th and 28th wk of gestation. A glucose screening test (GST) was performed with a 50-g glucose load, followed by a blood sample 1 h later. Patients with glucose levels  $> 140$  mg/dl 1 h after the GST were scheduled for a full oral glucose tolerance test (OGTT). One hundred seven patients had an abnormal GST, and 30 patients (4.3%) were diagnosed as having gestational diabetes mellitus (GDM). The percentage of GDM increased significantly when glucose levels were  $> 180$  mg/dl to a maximum of  $> 84.61\%$  when glucose levels were  $> 200$  mg/dl. Also, patient age was directly related to GDM, which increased in incidence to 20% when patients  $> 26$  yr. had an abnormal GST. After delivery, newborns weights were compared between those born to mothers with GDM ( $n = 30$ ) and those born to mothers with an abnormal GST ( $n = 77$ ). Patients with an abnormal GST and normal OGTT had 12 (15.58%) macrosomic and 2 premature newborns. However, patients with GDM had 5 (16.66%) macrosomic and no premature newborns. Patients with a normal GST had 7.33% of the macrosomic newborns. There was no perinatal mortality in newborns of GDM mothers; only 1 of the 5 macrosomic newborns presented transient hypoglycemia.

Evaluation of 26 GDM mothers; only 1 of the 5 macrosomic newborns presented transient hypoglycemia. Evaluation of 26 GDM patients was possible after delivery, disclosing 3 (11.53%) with non-insulin dependent diabetes mellitus and 5 (19.23%) with impaired glucose tolerance. These results showed 4.3% undetected GDM in our population and no differences in the proportion of macrosomic newborns between those born to mothers with GDM and those born to mothers with an abnormal GST.

**Sicree RA, Hoet JJ, Zimmet P, King HOM, Coventry JS.**

**The association of non-insulin dependent diabetes with parity and stillbirth occurrence amongst five Pacific populations.**

**Diab. Res. Clin Prac. 1986; 2: 113-122.**

Previous reports have shown the prevalence of non-insulin-dependent diabetes to be high amongst several populations living in the South and Central Pacific region, and a number of factors including a sedentary life-style, urban residence, obesity and genetic factors have been implicated in its aetiology. Amongst some populations increasing parity has been shown to be associated with abnormal glucose tolerance, but the cross sectional data available did not suggest any such association amongst the five Pacific Island populations surveyed.

Still birth rates are high amongst all these populations, particularly so amongst the older women, and several methods of analysis suggest that abnormal glucose tolerance is associated with a significantly increased risk of still birth. This association appears more marked amongst younger women in all populations, with the overall relative risk of a stillbirth occurrence for diabetic women aged less than 45 years being 2.6 (95% confidence interval being 1.4-4.8), and for women aged less than 45 years with impaired glucose tolerance being 2.2 (95% confidence interval being 1.3-3.7). As many of the women diabetic at the time of surveys would not have been during their pregnancies, these risk estimates are probably underestimates. Longitudinal studies may suggest even higher figures.

Nonetheless the results of these surveys suggest that the high prevalence of abnormal glucose tolerance in these populations may be at least partly responsible for their high levels of stillbirth occurrence.

**Kitzmilller JL, Gavin LA, Gin GD, Jovanovic-Peterson L, Main EK, Zigrang WD.**

**Preconception care of diabetes. Glycemic control prevents congenital anomalies.**

**JAMA 1991; 265: 731-36.**

To test the rule of intensive management of diabetes before and during early pregnancy, 84 women recruited prior to conception were compared with 110 women who were already pregnant reformed at 6 to 30 weeks gestation. All underwent daily measurement of fasting and postprandial capillary blood glucose levels. Mean blood glucose levels during embryogenesis and organogenesis were within 3.3 to 7.8 mmol/l in 50% of preconception subjects and exceeded 10 mmol/l in 6.5%. One major congenital anomaly occurred in 84 infants (1.2%) of women treated before conception compared with 12 anomalies in 110 infants (10.3%) of mothers in the postconception group. Transient symptomatic hypoglycemia occurred during embryogenesis in 60% of women in the preconception group, with a median frequency of 2.7 episodes per week, but was not associated with excess malformations. The authors conclude that education and intensive management for glycemic control of diabetic women before and during early pregnancy will prevent excess risk of congenital anomalies in their infants.

**Mille JL, Simpson JL, Driscoll SC, Jovanovic-Peterson R.**

**Incidence of spontaneous abortion among normal women and insulin dependent diabetic women whose pregnancies were identified within 21 days of conception.**

**N Engl J Med 1988;319:1617-23.**

To determine whether insulin dependent diabetes increases a women's risk of having a spontaneous abortion and to assess the relationship between metabolic control and loss of pregnancy in diabetics, 386 women with insulin-dependant diabetes and 432 non diabetic women were studied before or within 21 days after conception and followed prospectively.

Loss of pregnancy assessed in 62 diabetes women (16%) and in 70 non-diabetic women (16%). After adjustment for known risk factors for spontaneous abortion, the rate was still not significantly higher among diabetic women. However, among the diabetic women most of whom had good metabolic control, those who had spontaneous abortion had higher fasting and postprandial glucose levels in the first trimester than those whose pregnancies had good control prior to delivery. In the small subgroup of diabetic women with poor control, who had increased values for glycosylated hemoglobin in the first trimester each increase of 1% above the normal range was associated with an increase of 3.1% in the rate of pregnancy loss whether women with good metabolic control are no more likely to lose a pregnancy than non-diabetic women. However, diabetic women with increased blood glucose and glycosylated hemoglobin levels in the first trimester have a significantly greater risk of spontaneous abortion.

*Previous articles had suggested that diabetic women in poor metabolic control are more likely to have spontaneous abortions.*

*It was uncertain, however, whether the imperfect methods of treatment today were sufficient to prevent early fetal wastage. Considering that this report involved large number of patients, was well controlled, and used state of-the-art techniques one can be reasonably confident that the answer is affirmative.*

**Miodovnik M, Mimouni F, Siddiqi TA, Khoury J, Berk MA. Spontaneous abortions in repeat diabetic pregnancies: a relationship with glycemic control. Obstet Gynecol 1990;75:75-8.**

In previous studies, the authors reported a high rate of spontaneous abortions in insulin-dependent diabetic pregnancies. Abortions were associated with poor first trimester glycemic control. The authors hypothesized that improvement of glycemic control from one pregnancy to the other would improve fetal outcome and that deterioration of glycemic control would increase the likelihood of abortion. They studied prospectively 43 insulin dependent diabetic women (White class B-RF) with 2 consecutive pregnancies, recruited before 9 weeks gestation. Preprandial and 90 minute postprandial blood glucose concentrations were measured at each weekly visit. HBA<sub>1c</sub> was measured at 9 weeks' gestation. Twenty women had 2 successful pregnancies and 15 had an abortion followed by a successful pregnancy (abortion-no abortion); the sample sizes for other sequences (no abortion-abortion, n = 5; and abortion-abortion, n = 3) were too small to allow for analysis. HBA<sub>1c</sub> concentrations were stable in the sequence no abortion-no abortion (9.7% ± 0.5% vs. 9.8% ± 0.4%, mean ± SEM; not significant), whereas in the sequence abortion-no abortion, there was a significant decrease in glycohemoglobin A values from the non-successful to the successful pregnancy (10.7% ± 0.6% vs. 9.3% ± 0.4%; p=0.01). Similarly, in the sequence abortion-no abortion, there was a significant decrease in mean postprandial blood glucose from first to second pregnancy (166 ± 13 mg/dl vs. 135 ± 11mg/dl; p = 0.04), whereas in the sequence no abortion-no abortion, mean postprandial blood glucose did not change significantly (160 ± 14 mg/dl vs. 144 ± 11 mg/dl; not significant).

**Menon RK, Cohen RM, Sperling MD, Cutfield WS, Mimouni F, Khoury JC. Transplacental passage of insulin in pregnant women with insulin dependent diabetes mellitus. Its role in fetal macrosomia. New Engl J Med. 1990;323:309-15.**

Foetal macrosomia occurs despite nearly normal maternal blood glucose levels in women with diabetes treated with insulin. The authors examined the hypothesis that it may be caused by insulin transferred as an insulin antibody complex from the mother to her fetus. They adapted and validated a method based on high performance liquid chromatography and used it to quantitate insulin in small volumes (0.5 to 1.0 ml) of cord serum from 51 infants born to mothers with insulin dependent diabetes mellitus. In mothers receiving only human insulin (n=6), only human insulin was detected in cord serum. Of the remaining 45 infants, whose mothers received animal insulin during pregnancy, 28 (group 1) had levels of animal (bovine or porcine) insulin (mean [± SE], 707 + 163 pmol per liter) that constituted 27.4 ± 2.5 percent of the total insulin concentration (2393 ± 500 pmol per liter) measured in the cord serum. The cord serum insulin concentration in the remaining 17 infants (group 2), in whom only human insulin was detected (381 ± 56 pmol per liter), was only 15 percent of that in group 1 (p <0.01). There was a significant correlation between the maternal and the cord serum concentration of anti insulin antibody and the concentration of animal insulin in the baby (r=0.77, p <0.01, and r=0.76, p <0.001, respectively), suggesting that the animal insulin was transferred as an insulin antibody complex. In group 1, the mean concentration of animal insulin in cord serum was higher in the 12 infants with macrosomia than in the 16 infants without the condition (1113 ± 321 vs. 402 ± 110 pmol per liter; p <0.05), and the concentration of animal insulin in cord serum correlated with both weights (r=0.39, p <0.05). The maternal glycosylated hemoglobin values and the incidence of respiratory distress syndrome were similar in groups 1 and 2. The authors concluded that considerable amounts of antibody bound insulin are transferred from mother to foetus during pregnancy in some women with insulin dependent diabetes mellitus; the extent of transfer correlates with the maternal concentration of anti-insulin antibody. The correlation between macrosomia and the concentrations of animal insulin in cord serum indicates that the transferred insulin has biologic activity and suggests that the formator of antibody to insulin in the mother is a determinant of fetal outcome independent of maternal blood glucose levels.

*This study offers a possible explanation for the fact that about 20 percent of mothers in whom nearly normal glycemia is maintained during pregnancy deliver infants who have macrosomia. It reinforces the recommendation of using insulins of lowest immunogenicity in treating women with IDDM before and during their child-bearing years.*

**Becerra JE, Khoury MJ, Cordero JF, Erickson JD. Diabetes mellitus during pregnancy and the risks for specific birth defects: a population based case control study. Pediatrics 1990; 85: 1-9.**

Although the excess risk of birth defects among children of mothers with diabetes mellitus is well documented, there are few data concerning the risk of specific malformations. In the Atlanta Birth Defects Case-Control Study, those risks for malformations were evaluated. The population based study included 4,929 live and stillborn babies with major malformations ascertained by the Metropolitan Atlanta Congenital Defects Program in the first year of life born to residents of Metropolitan Atlanta between 1986 and 1990. The study also included 3,029 non malformed live babies who were frequency matched to case babies by race, period of birth, and hospital of birth. The relative risk for major malformations among infants of mothers with insulin dependent diabetes mellitus (n = 28) was 7.9 (95% confidence interval [CI] 1.9, 33.5) compared with infants of non-diabetic mothers. The relative risks for major central nervous system and cardiovascular system defects were 15.5 (95% CI = 3.3, 73.8) and 18.0 (95% CI = 3.9, 82.5), respectively. The absolute risks for major, central nervous system, and cardiovascular system malformations among infants of diabetic mothers were 18.4, 5.3, and 8.5 per 100 live births, respectively. Infants of mothers with gestational diabetes

mellitus who required insulin during the third trimester of pregnancy were 20.6 (95% CI = 2.5, 168.5) times more likely to have major cardiovascular system defects than infants of non diabetic mothers. The absolute risk for infants of this group of diabetic mothers was 9.7%. No statistically significant differences were found among infants of mothers with gestational diabetes mellitus who did not require insulin during pregnancy.

#### **FOLLOW-UP**

**Ali Z, Alexis JD.**

**Occurrence of diabetes mellitus after gestational diabetes mellitus in Trinidad.**

**Diabetes Care 1990;13:527-29.**

This study was undertaken to determine the incidence of diabetes mellitus (DM) and impaired glucose tolerance (IGT) after gestational diabetes mellitus (GDM). It is a follow-up study of a consecutive sample of women with GDM who delivered in the hospital between June 1981 and December 1984. Of these, a volunteer sample of 60 women (38%) consented to participate 3.5- 6.5 yr. later. The two groups were remarkably similar in ethnic composition, mean age at index delivery, marital status, and family history of DM. Interviews revealed that 26 women receiving treatment. The remaining 34 women (37%) were given a 2-h 75-g oral glucose tolerance test, and fasting and half-hourly venous blood samples were obtained and analyzed for plasma glucose. Based on accepted diagnostic criteria, 11 (32%) of 34 had DM, 10 (29%) had IGT, and 13 (38%) had normal glucose tolerance. A total of 37 (62%) of 60 women had developed DM, and another 10 (17%) had IGT in the intervening 3.5-6.5 yr. The results support findings that GDM is associated with an increased risk of mothers developing DM in later life.

*Workers from East Germany, Australia and Saudi Arabia have reported similar high incidence of impaired glucose tolerance during 1-2 years of post partum follow-up. Increased age, fasting plasma glucose >105 mg/dl and relative insulinopenia may serve as prognostic indicator of childhood of impaired glucose tolerance or frank diabetes mellitus during post partum follow-up atleast in GDM class A1 or A2.*

**Oats JN, Beischer NA.**

**The persistence of abnormal glucose tolerance after delivery.**

**Obstet. Gynecol. 1990;75:397-401.**

In the first 7 days after delivery, 270 women who had gestational diabetes and 100 who had normal prenatal glucose tolerance were retested for glucose intolerance. In the group who had gestational diabetes, glucose tolerance remained abnormal by the Mercy Maternity Hospital criterion in 28% those who had been delivered vaginally and in 43% of those delivered by caesarean. The only abnormal test in the control group was in 1 of the 2 women delivered by caesarean, and this test returned to normal by the 7th postoperative day. By 6 weeks postpartum, the incidence of abnormal glucose tolerance was 24% and 30% for patients having vaginal and abdominal deliveries, respectively. The method of infant feeding had no significant influence on the prevalence of

abnormal glucose tolerance. The authors conclude that if a glucose tolerance test has not been performed prenatally, the test is still worthwhile in the immediate puerperium if the possibility of gestational diabetes has been raised by adverse pregnancy outcome, because about 1 in 3 diabetic patients will be thus identified. However, screening in the puerperium is not a substitute for prenatal screening.

*In general, all women with GDM should receive post partum assessment of glucose tolerance within six weeks to three months following delivery. Those with persistent abnormality should be classified as having pregestational diabetes mellitus or impaired glucose tolerance during future pregnancies.*

**Pettitt DJ, Aleck KA, Baird HR, Carrahier MJ, Bennett PSS, Knowler WC.**

**Congenital susceptibility to NIDDM. Role of intrauterine environment.**

**Diabetes 1988;37:622-28.**

Non-insulin-dependent diabetes mellitus (NIDDM) during pregnancy in Pima Indian women results in offspring who have a higher prevalence of NIDDM (45%) at age 20-24 yr. than in offspring of non-diabetic women (1.4%) or offspring of pre-diabetic women (8.6%), i.e. women who developed diabetes only after the pregnancy. These differences persist after taking into account paternal diabetes, age at onset of diabetes in the parents, and the offspring's weight relative to height. The findings suggest that the intrauterine environment is an important determinant of the development of diabetes and that its effect is in addition to effects of genetic factors.

**Pettitt DJ, Knowler WC, Bennett PH, Aleck KA, Baird HR.**

**Obesity in offspring of diabetic Pima Indian women despite normal birth weight.**

**Diabetes Care 197;10:76-80.**

The relationships of birth weight and maternal diabetes to the development of obesity were examined at 5-19 yr. of age in the offspring of Pima Indian women. At each age, offspring of diabetic women, even those who were of normal birth weight had a higher mean weight relative to height than offspring of nondiabetic and prediabetic women. Birth weight was predictive of relative weight in 5 to 9 and 10 to 14 yrs old offspring of nondiabetic women but not in the oldest group. In contrast, for offspring of prediabetic and diabetic women, birth weight was not predictive of subsequent obesity at any age studied. Offspring of diabetic women were heavier than offspring of non-diabetic and pre-diabetic women regardless of birth weight. Thus, maternal diabetes was important in predicting body size in the offspring even after accounting for the effects of the birth weight and maternal body size.

*According to Fienkel, abnormal fuel delivery in vitro can modify phenotypic gene expression in certain cells during key phase, of their intrauterine organisation, replication, differentiation and/or functional maturation.*