

Maternal Glucose Concentration Influences Fetal Growth, Gestation, and Pregnancy Complications

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Using 1990–1995 data, the authors examined the influence of post-challenge maternal glucose concentration on pregnancy outcome in 1,157 nondiabetic US gravidas. After control for potential confounding variables and comparing gravidas with lower glucose concentrations (<99 mg/dl) with the others, they found that mean birth weight increased by 50 g and 200 g with glucose concentrations of 99–130 mg/dl and >130 mg/dl, respectively. Increased maternal glucose concentration also was associated with an increased risk of large-for-gestation fetuses (p for trend < 0.001) and a decreased risk of fetal growth restriction (p for trend < 0.05). The association between glucose and gestation was inverse and significantly shortened when glucose concentrations were higher. Maternal complications increased twofold or more with high glucose concentrations and included cesarean section and clinical chorioamnionitis. Chorioamnionitis in combination with high maternal glucose concentration increased the risk of very preterm delivery almost 12-fold. These observations extend Pedersen's hypothesis—that high concentrations of maternal glucose give rise to increased nutrient transfer to the fetus and increase fetal growth, beyond the model of maternal diabetes (*Acta Endocrinol* 1954;16:330–42). They raise the question of whether higher, but seemingly normal maternal glucose concentration predisposes to or is a marker for placental inflammation and infection. *Am J Epidemiol* 2001;154:514–20.

birth weight; cesarean section; chorioamnionitis; gestational age; glucose; hypertension; pregnancy complications; pregnancy outcome

Glucose is the main energy substrate for intrauterine growth and is transmitted in a steady stream from mother to fetus (1–3). Glucose is produced as a result of maternal metabolism principally from carbohydrate in the diet and from the gluconeogenic amino acids. The hormone insulin, in turn, regulates glucose.

Pedersen hypothesized that in maternal diabetes, high concentrations of glucose give rise to increased nutrient transfer to the fetus (4). To prevent fetal hyperglycemia, fetal insulin secretion and fetal growth increase. This relation is supported by observations of gestational and pregestational diabetes that higher maternal glucose concentrations, particularly after a meal, predict greater infant birth weight (5–7). Conversely, maternal hypoglycemia also has been associated with an increased risk of fetal growth restriction (8, 9).

It seems reasonable that a relation between maternal glucose and fetal growth also should exist in women who do not have diabetes. However, such studies (10–15) generate controversy (e.g., refer to Jarrett (16)) in part because glucose is the primary focus, and there is little control for factors that potentially confound the relation between glucose and fetal growth.

There is another underlying issue. While higher maternal glucose concentrations may lead to increased fetal growth, they also are associated with pregnancy complications when the mother has diabetes (17). A smaller literature also suggests that among nondiabetic gravidas, higher glucose concentrations are associated with increased operative delivery as well as pregnancy-induced hypertension (11, 13–15). We wanted to determine whether these relations were present in our data and whether a higher glucose concentration also was associated with chorioamnionitis. Chorioamnionitis is a manifestation of subclinical infection(s) associated with preterm delivery (18). Consequently, we examined the influence of maternal glucose concentration on the course and outcome of pregnancy in gravidas without a diagnosis of either gestational or pregestational diabetes.

MATERIALS AND METHODS

The Camden Study (e.g., refer to Scholl et al. (19, 20)) is a prospective study of the effect of risk factors during pregnancy in young, generally healthy women residing in Camden, New Jersey, one of the poorest cities in the United

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Abbreviation: BMI, body mass index.

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States. Participants include young (aged ≤ 18 years) and more mature (aged 19–29 years) pregnant women enrolling for prenatal care in Camden clinics. There is increased recruitment of subjects aged 18 years or less to study the development of young women who are pregnant. Gravidas with serious nonobstetric problems (e.g., lupus, chronic hypertension, diabetes mellitus type 1 or type 2, seizure disorders, malignancies, drug or alcohol abuse) are not eligible. In our analysis of 1990–1995 data, the rate of loss to follow-up between entry to care (on average at 16 weeks' gestation) and the postpartum period (4–6 weeks) was 6.6 percent.

We confined this analysis to gravidas without gestational diabetes who had singleton pregnancies that resulted in live-born infants. Socioeconomic, demographic, and lifestyle data were obtained by interview at entry to care and were updated during pregnancy and the postpartum period (4–6 weeks). Maternal weight was measured at each visit and height at entry to prenatal care; pregravid weight was obtained by recall. Skinfolds (triceps, subscapular) were measured at entry, at week 28, and in the postpartum period at 4–6 weeks. Adequacy of gestational weight gain for the whole of pregnancy was defined to within 2 completed weeks of delivery by using published criteria that adjust weight gain for duration of gestation (21). Body mass index (BMI) was computed as pregravid weight for height squared (kg/m^2).

Information on current and past pregnancy outcomes, complications, and infant abnormalities was abstracted from the prenatal records, the delivery record, delivery logbooks, and the infant's chart. Pregnancy outcomes included preterm delivery (<37 completed weeks or <259 days), moderate preterm delivery (33– <37 completed weeks or 231–258 days), and very preterm delivery (≤ 32 completed weeks or <231 days). A large-for-gestational-age fetus was defined by a birth weight for gestation above the 90th percentile of Brenner's standard (22), which adjusts for maternal parity, ethnicity, and fetal sex. Fetal growth restriction was defined by a birth weight for gestation below the 10th percentile of the same standard. Gestation duration was based on the gravida's last normal menstrual period and was confirmed or modified by ultrasound. Complications included delivery by cesarean, pregnancy-induced hypertension (diastolic blood pressure of >90 mmHg), and clinical chorioamnionitis (two or more of the following: uterine contractions, fever, maternal or fetal tachycardia, uterine tenderness, foul-smelling discharge or amniotic fluid, leukocytosis (23)).

Maternal plasma glucose was examined in 1,157 gravidas without a diagnosis of diabetes (type 1 or type 2) who received a 1-hour, 50-g glucose screening test to detect gestational diabetes (17). In Camden, this test is routinely conducted in all gravidas between 24 and 28 weeks of gestation. Women who had plasma glucose concentrations of >140 mg/dl received a 3-hour, 100-g oral glucose tolerance test, and those testing positive for gestational diabetes were excluded from this analysis. After this exclusion, the sample median (99 mg/dl) for the 50-g glucose screening test was used as a cutpoint, with an additional stratum consisting of gravidas without a diagnosis of gestational diabetes but with glucose concentrations suggesting hyperglycemia (>130 mg/dl) (24, 25).

Confounding was assessed by comparing crude and adjusted odds ratios or regression coefficients. By using multiple logistic regression, we fit separate models for each outcome containing the independent variable(s), maternal age, parity, and potential confounding variables (26); two-way interactions with glucose also were examined. Adjusted odds ratios and their 95 percent confidence intervals were computed from the logistic regression coefficients and their corresponding covariance matrices. In logistic models, the significance of the linear trend was assessed across the categories of glucose coded as an ordinal-level variable. Multiple linear regression or analysis of variance was used when the dependent variable was continuous.

RESULTS

Our study population comprised primarily young and minority women; for more than 85 percent, their pregnancy care was funded by Medicaid. A total of 3.8 percent were diagnosed with gestational diabetes during their current pregnancy and were therefore excluded from this analysis.

Little association was found between maternal glucose concentration, ethnicity, parity, smoking, or other important risk factors often related to the outcome of pregnancy (table 1). However, prenatal care funding from sources other than Medicaid was associated with higher glucose concentrations. Women who did not receive Medicaid were older than those who did (44.1 percent were aged 19–29 years vs. 27.0 percent). When examined as a continuous variable, maternal age and glucose were weakly but positively correlated (Spearman's $\rho = 0.09$, $p < 0.01$). More importantly, increased maternal pregravid BMI and larger summed skinfolds (triceps plus subscapular) were associated with higher glucose concentrations at entry to care and at week 28.

Higher maternal glucose was associated with increased infant birth weight (table 2). No significant interaction was found between maternal glucose and pregravid BMI (p for interaction > 0.50). Controlling for potential confounding variables (age, parity, ethnicity, clinic payment status, smoking, pregravid BMI, gestational weight gain, prior low birth weight, and duration of gestation) and comparing women whose plasma glucose concentrations were <99 mg/dl with the others indicated that birth weights were approximately 50 g higher ($p < 0.05$) for gravidas whose glucose concentrations were 99–130 mg/dl and 200 g higher ($p < 0.005$) for those with glucose concentrations of >130 mg/dl. The difference in birth weight for women whose glucose concentrations were >130 mg/dl versus above the median was 140 g ($p < 0.05$).

On the other hand, increasing maternal plasma glucose concentration was associated with decreasing duration of gestation (table 2). When we controlled for potential confounding variables, a comparison of women with lower glucose concentrations (<99 mg/dl) indicated that gestation was approximately 1.8 days shorter ($p < 0.05$) for gravidas with glucose concentrations of 100–130 mg/dl and 4.8 days shorter ($p < 0.01$) for glucose concentrations of >130 mg/dl.

As expected, glucose concentration was related to fetal growth. After control for potential confounding variables,

TABLE 1. Background characteristics of gravidas according to maternal glucose concentration, the Camden Study, United States, 1990–1995

Characteristic	Glucose concentration (mg/dl)		
	<99 (<i>n</i> = 574)	99–130 (<i>n</i> = 502)	>130 (<i>n</i> = 81)
Interquartile glucose range (mg/dl)	77–92	104–118	133–145
Age group (%)			
<16 years	29.3	27.1	25.9
16–18 years	45.6	40.8	40.7
≥19 years	25.1	32.1	33.3
Parous (%)	28.4	30.9	30.9
Ethnicity (%)			
Black	59.1	55.4	48.2
Hispanic (Puerto Rican)	31.7	35.5	37.0
White	9.2	9.2	14.8
No. of cigarettes smoked/day (%)			
0	79.8	80.3	74.1
1–9	14.5	14.5	18.5
10–19	4.0	4.0	2.5
≥20	1.7	1.2	5.0
Receipt of Medicaid (%)	90.2	90.6	81.5*
Pregravid body mass index (kg/m ²) (mean (SD)†)	23.2 (4.6)	23.9 (4.9)	25.0 (6.1)**
Inadequate gestational weight gain (%)	22.8	19.9	19.8
Sum of skinfolds‡ (mm) (mean (SD))			
Entry to prenatal care	37.1 (16.1)	40.6 (16.0)	44.1 (20.1)**
Week 28	39.6 (15.1)	43.1 (16.8)	46.6 (20.4)**
Prior preterm delivery§ (%)	8.9	16.8	4.0*
Prior low birth weight¶ (%)	9.8	16.8	0.0*
Anemia¶ (%)			
Entry to prenatal care	19.9	22.4	20.3
Week 28	58.8	57.0	56.9
Gestation at entry to care (no. of weeks (SD))	16.2 (6.4)	16.2 (6.2)	16.2 (6.7)

* $p < 0.05$; ** $p < 0.001$ for overall F test or chi-square statistic.

† SD, standard deviation.

‡ Sample sizes were 555 (<99 mg/dl), 490 (99–130 mg/dl), and 78 (>130 mg/dl); entry skinfolds were adjusted for duration of gestation.

§ Confined to parous women, sample sizes were 163 (<99 mg/dl), 155 (99–130 mg/dl), and 25 (>130 mg/dl).

¶ Sample sizes were 422 (<99 mg/dl), 379 (99–130 mg/dl), and 59 (>130 mg/dl).

higher glucose concentrations were associated with significant linear trends for decreased risk of fetal growth restriction and for increased risk of large-for-gestation fetuses (table 3). Higher glucose concentrations also were related to an increasing risk of preterm delivery, but confidence intervals were wide and included unity (table 3).

After control for potential confounding variables, significant linear trends were found for cesarean delivery, new cesarean delivery, and clinical chorioamnionitis, but not pregnancy-induced hypertension, to occur more often at higher concentrations of maternal glucose (table 4). Except for pregnancy-induced hypertension, higher maternal glucose concentration (>130 mg/dl) was associated with a twofold or greater risk of each of these complications (table 4).

Risk of very preterm delivery was significantly increased for gravidas with clinical chorioamnionitis (adjusted odds ratio = 3.43, 95 percent confidence interval: 1.22, 9.65 after control for age, parity, ethnicity, number of cigarettes smoked/day, pregravid BMI, gestational weight gain, and prior preterm delivery). However, this effect depended on concentration of maternal glucose. For gravidas with chorioamnionitis and high glucose concentrations (>130 mg/dl), risk of very preterm delivery was increased nearly 12-fold (table 5). For women with chorioamnionitis and lower glucose concentrations, risk of very preterm delivery was increased somewhat, but the 95 percent confidence interval included unity. There was no association between clinical chorioamnionitis and moderately preterm delivery and no relation with or effect modification by maternal glucose (table 5).

TABLE 2. Association between infant birth weight, duration of gestation, and maternal glucose concentration, the Camden Study, United States, 1990–1995

Glucose concentration (mg/dl)†	No.	Infant birth weight (g)‡		Duration of gestation (days)‡	
		Mean	SEM§	Mean	SEM
<99	574	3,105.50	16.62*	271.81	0.63**
99–130	502	3,160.24	17.72***	269.99	0.63
>130	81	3,304.97	44.41	266.98	1.61

* $p < 0.05$ vs. 99–130 mg/dl; $p < 0.001$ vs. >130 mg/dl; ** $p < 0.05$ vs. 99–130 mg/dl; $p < 0.01$ vs. >130 mg/dl; *** $p < 0.01$ vs. >130 mg/dl.

† Interquartile ranges for glucose: 77–92 mg/dl (glucose <99 mg/dl), 104–118 mg/dl (glucose 99–130 mg/dl), and 133–145 mg/dl (glucose >130 mg/dl).

‡ Adjusted for age; parity; ethnicity; pregravid body mass index; gestational weight gain; no. of cigarettes smoked/day; clinic pay status; or prior low birth weight or preterm delivery, as appropriate. Birth weight model was also adjusted for duration gestation.

§ SEM, standard error of the mean.

DISCUSSION

During the first half of pregnancy, energy from the maternal diet is stored in the form of fat; greater insulin sensitivity is thought to be the stimulus (1, 2). By the third trimester, increasing insulin resistance triggers the cessation of fat accretion, the lipolysis of stored fat, and the release of free fatty acids from those stores (1, 2). Free fatty acids are an alternative metabolic fuel for the mother and are thought to

diminish her glucose utilization and help preserve glucose from the maternal diet for use by the fetus (1, 2, 27). Increasing insulin resistance in skeletal muscle and the liver, which reduces glucose uptake and increases hepatic glucose production, is a maternal adaptation to the fuel needs of the rapidly growing fetus (3).

In diabetes, this process is amplified, and higher concentrations of maternal glucose and other metabolic fuels (triglycerides, amino acids, free fatty acids, ketones) are transported to the fetus (1, 2). Per Pedersen's hypothesis (4), the fetus responds by making more insulin, adding fat, and gaining weight. Thus, with maternal diabetes (5), a positive effect of third-trimester nonfasting maternal glucose was noted on infant birth weight, after adjustment for maternal body mass, smoking, and glucose from prior trimesters.

Overweight and obese nondiabetic women have larger infants and an increased risk of delivering a macrosomic fetus (28). Along with greater plasma volume and the increased placental perfusion associated with obesity, this relation is likely to reflect greater maternal insulin resistance, with diminished glucose disposal leaving more glucose for fetal growth (29). For example, with increasing BMI, gravidas who are not diabetic have higher glucose concentrations on the standard 50-g screening test (30), a finding also confirmed in the present study with pregravid BMI and the summed skinfolds (triceps plus subscapular) at entry to prenatal care and at week 28.

Camden gravidas with higher concentrations of glucose gave birth to infants of significantly higher birth weights than did women with lower glucose concentrations. The

TABLE 3. Association of maternal glucose concentration with fetal growth restriction and with large-for-gestational-age, preterm, and very preterm delivery, the Camden Study, United States, 1990–1995

Glucose concentration (mg/dl)	No.	Fetal growth restriction*			Large for gestational age*			Preterm delivery*			Very preterm delivery*		
		%†	AOR‡	95% CI‡	%†	AOR	95% CI	%†	AOR	95% CI	%†	AOR	95% CI
<99	574	6.97	1.00		8.01	1.00		10.63	1.00		2.61	1.00	
99–130	502	5.98	0.76	0.45, 1.24	11.98	1.40	0.92, 2.12	12.95	1.14	0.79, 1.67	2.99	1.14	0.54, 2.40
>130	81	1.23	0.16	0.02, 1.21	22.22	3.59	1.90, 6.78	14.81	1.51	0.77, 2.98	3.70	1.75	0.48, 6.36
<i>p</i> for trend		<0.05			<0.001			<0.15			<0.40		

* Adjusted for age; parity; ethnicity; no. of cigarettes smoked/day; pregravid body mass index; clinic pay status; gestational weight gain; prior low birth weight or preterm delivery, as appropriate. Growth restriction and large-for-gestational-age models were also adjusted for fetal sex.

† Unadjusted proportion with outcome of interest.

‡ AOR, adjusted odds ratio; CI, confidence interval.

TABLE 4. Association of maternal glucose concentration and maternal complications with cesarean section, clinical chorioamnionitis, and pregnancy-induced hypertension, the Camden Study, United States, 1990–1995

Glucose concentration (mg/dl)	No.	Cesarean section*			New cesarean section*			Chorioamnionitis*			Pregnancy-induced hypertension*		
		%†	AOR‡	95% CI‡	%†	AOR	95% CI	%†	AOR	95% CI	%†	AOR	95% CI
<99	574	11.67	1.00		8.54	1.00		5.40	1.00		8.54	1.00	
99–130	502	14.14	1.18	0.82, 1.70	11.55	1.31	0.87, 1.97	6.97	1.29	0.77, 2.14	9.56	1.04	0.68, 1.59
>130	81	22.22	2.08	1.15, 3.70	19.75	2.64	1.41, 4.97	17.28	4.13	2.06, 8.28	7.41	0.55	0.19, 1.59
<i>p</i> for trend		<0.05			<0.01			<0.001			<0.90		

* Adjusted for age, parity, ethnicity, no. of cigarettes smoked/day, pregravid body mass index, and gestational weight gain.

† Unadjusted proportion with complications of interest.

‡ AOR, adjusted odds ratio; CI, confidence interval.

TABLE 5. Association of very preterm, moderately preterm, and all preterm delivery with plasma glucose concentration and clinical chorioamnionitis, the Camden Study, United States, 1990–1995

Glucose concentration (mg/dl)	Chorioamnionitis						
	Yes				No		
	No.	%*	AOR†	95% CI†	No.	%*	AOR
<i>Very preterm delivery‡</i>							
<99	31	3.23	1.50	0.19, 11.82	543	2.6	} 1.00
99–130	35	5.71	3.02	0.66, 13.89	467	2.8	
>130	14	14.29	11.88	2.24, 62.81	67	1.5	
<i>Moderately preterm delivery‡</i>							
<99	31				543	8.66	} 1.00
99–130	35	8.57	0.82	0.24, 2.75	467	10.06	
>130	14				67	13.43	
<i>All preterm delivery‡</i>							
<99	31	3.23	0.24	0.03, 1.82	543	11.05	} 1.00
99–130	35	14.29	1.23	0.46, 3.26	467	12.85	
>130	14	14.29	1.27	0.28, 5.80	67	14.93	

* Unadjusted proportion of infants delivered very preterm, moderately preterm, or preterm.

† AOR, adjusted odds ratio; CI, confidence interval.

‡ Adjusted for age, parity, ethnicity, clinic pay status, no. of cigarettes smoked/day, gestational weight gain, pregravid body mass index, and prior preterm delivery.

association of glucose with birth weight persisted after adjustment for pregravid BMI and other variables. For gravidas with glucose concentrations below the median (<99 mg/dl), the difference in birth weight was small, amounting to approximately 50 g when compared with those above the median. However, with higher glucose concentrations (>130 mg/dl), the differences were substantial: approximately 160–200 g in birth weight. Consistent with this finding, in logistic regression analysis there were significant linear trends for increasing maternal glucose concentration to be associated with an increasing trend for risk of large-for-gestation fetuses and with a decreasing trend in risk for fetal growth restriction. Thus, it is possible that women in the current study who had higher postload glucose concentrations had chronically higher glucose concentrations after eating. Increased postprandial glucose may have contributed to the increased growth of their fetuses.

Maternal glucose concentration is influenced by the maternal diet, particularly by energy (2, 31) and/or carbohydrate (32). This finding has been studied mainly in diabetic pregnancy, when restriction alters metabolic fuels that correlate with fetal growth (2). In the classic study of wartime famine (33), in which well-nourished Dutch women experienced a serious food shortage during the course of pregnancy, the authors observed that 1) maternal weight decreased; 2) infant birth weight declined; 3) the largest deficits in birth weight, approximately 300 g, occurred with exposure to famine during the last half of pregnancy; and 4) birth weight returned to usual after the famine ended. It is likely that a change in maternal glucose concentration was one of the underlying factors.

A gravida's reduced intake of nutrients as a result of smaller or less-frequent meals during a famine should result in lower circulating concentrations of maternal glucose. Reductions in maternal body mass and fat stores from famine should alter maternal glucose disposal and leave less fat to oxidize as an alternative maternal fuel. Thus, a reduced glucose stream from mother to fetus would result in slower fetal growth, smaller birth size, and an increased risk of fetal growth restriction. Apart from war, famine, or diabetes, low concentrations of maternal glucose have been associated with an increased risk of fetal growth restriction (8, 9).

Camden gravidas with higher glucose concentrations had a shorter duration of gestation (2–5 days) in comparison to gravidas whose glucose concentrations were low (<99 mg/dl). After control for potential confounding variables, higher maternal glucose concentration was associated with a greater risk of pregnancy complications (cesarean section, new cesarean section, clinical chorioamnionitis) that often result in or accompany very preterm delivery. Thus, in gravidas without diabetes, a higher postload maternal glucose concentration may, on one hand, result in increased infant growth but, on the other hand, be a risk factor or a marker for a complicated pregnancy.

There have been several reports of positive associations of maternal plasma glucose concentration with increased risks of fetal macrosomia, toxemia, and cesarean section in women without diabetes (10–15). For example, Sermer et al. (13) examined the predictive ability of maternal glucose in more than 3,500 nondiabetic women from Toronto, Canada. After control for some potential confounding variables, they

concluded that a higher maternal glucose concentration predicted increased fetal macrosomia and cesarean section. Farmer et al. (14) found that, in women without diabetes, diminished maternal glucose disposal correlated with infant birth weight, length, and skinfolds ($n = 900$). Neonatal morbidity, including a trend in signs suggesting sepsis in the infant, increased when maternal glucose concentration was at the high end of the spectrum. However, to our knowledge ours is the first report to show that high maternal glucose concentration is associated with a complication that often presages neonatal sepsis, clinical chorioamnionitis in the mother.

Chorioamnionitis is associated with preterm delivery in general but primarily with early deliveries between 24 and 34 weeks of gestation (18, 34, 35). In agreement with this research, our study found that only very preterm delivery was associated with clinical chorioamnionitis. When clinical chorioamnionitis was accompanied by a high maternal glucose concentration, risk of very preterm delivery was increased about 12-fold.

Stress (infection, inflammation, trauma, psychological distress) raises plasma glucose concentrations by increasing the contrainsulin hormones (e.g., cortisol, placental growth hormone). Consequently, one possibility is that high glucose concentrations may be a risk factor or a risk marker for the subclinical infection that gives rise to chorioamnionitis. Unlike plasma glucose, amniotic fluid from women with intrauterine infection has a low glucose concentration (18, 36). Another possibility is that high maternal glucose concentrations may prompt additional testing, thus disproportionately increasing detection of chorioamnionitis and elevating the odds ratio in the subset of women with high glucose concentrations.

Much subclinical infection associated with very preterm delivery is manifested as a systemic inflammatory response that is otherwise asymptomatic (18). There is a small, but growing literature suggesting that, in adults, insulin resistance is an indicator of inflammation driven by interleukin-1, interleukin-6, and tumor necrosis factor α (37, 38). Chronic subclinical inflammation (elevated C-reactive protein) is increased in nondiabetic subjects with insulin resistance syndrome (39). Increased levels of C-reactive protein and the cytokines interleukin-6 and tumor necrosis factor α all are biomarkers or risk factors for preterm and very preterm delivery (40). Obese gravidas, who are more likely to be insulin resistant, have an increased risk of chorioamnionitis during pregnancy (28, 41). In the Collaborative Perinatal Project, Naeye reported that an increased risk of very preterm delivery was associated with acute chorioamnionitis among obese gravidas (41).

Finally, as this study has demonstrated, even minor degrees of hyperglycemia are associated with adverse outcomes and complications during pregnancy. Recommendations for initiating the 3-hour oral glucose tolerance test for diabetes during pregnancy at lower concentrations of glucose as well as with ethnic-specific cutpoints have been proposed (25, 42).

In summary, these observations regarding Camden gravidas extend Pedersen's hypothesis (4)—that high concentrations of maternal glucose give rise to increased nutrient transfer to the fetus and to increased fetal growth—beyond

the original model of maternal diabetes. They raise questions about whether higher but seemingly normal maternal plasma glucose concentrations are associated with very preterm delivery by predisposing to or acting as a marker for placental inflammation and subclinical infection. Finally, they suggest that insulin resistance in the urban poor might be an underlying cause of their increased risk of very preterm delivery.

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