

# The Fidgety Fetus Hypothesis

Fetal activity is an additional variable in determining birth weight of offspring of women with diabetes

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**OBJECTIVE** — To determine whether some offspring of women with diabetes are intrinsically more active than others in utero and whether those who are active are able to normalize their birth weight despite maternal hyperglycemia.

**RESEARCH DESIGN AND METHODS** — We conducted a three-phase study to view the relationship between fetal movements and subsequent birth weight in women with diabetes. Phase I was designed to assess maternal perception of fetal movements in a population of 10 women with diabetes. To improve our fetal monitoring techniques, in phase II we analyzed fetal movements using the Card Guard home fetal monitoring device (CG 900P) in a population of 13 women with gestational diabetes mellitus (GDM). To apply our observations of fetal movements to a larger population, during phase III we conducted a retrospective analysis of fetal monitoring strips (HP 8041A) from 46 women with GDM to examine the relationship between fetal heart rate (FHR) accelerations and percentile birth weight, corrected for gestational age.

**RESULTS** — Phase I confirmed that there is little variability in fetal movements (i.e., fetal kicks did not significantly deviate from one another on a day-to-day basis). In phase II, the fetal monitoring strips illustrated that the active fetuses (defined as  $\geq 4$  FHR accelerations in a 20-min period) were always active, and the inactive fetuses were always inactive. The mean birth weight percentile, corrected for gestational age, in the active group was 37 vs. 63% in the inactive group ( $P = 0.05$ ). In phase III, the fetal monitoring strips showed an inverse correlation between the mean number of FHR accelerations and the birth weight of the fetus, corrected for gestational age. The mean birth weight percentile in the active group was 37 vs. 62% in the inactive group ( $P = 0.0017$ ).

**CONCLUSIONS** — The fetus appears to play a role in determining its own destiny. Increased fetal activity may minimize the impact of hyperglycemia on subsequent birth weight. The inactive fetus appears to be at a higher risk for glucose-mediated macrosomia.

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**M**aternal glucose concentration plays a major role in the birth weight of infants born to women with gestational diabetes mellitus (GDM). deVeciana et al. (1) reported that women with GDM who only monitor preprandial glucose have a 42% risk of neonatal macrosomia, whereas those who monitor both preprandial and 1-h postprandial

glucose decrease their risk of neonatal macrosomia to near normal. Macrosomia, defined as birth weight  $>90$ th percentile for gestational age, ethnicity, and sex, is associated with an increased risk of birth trauma, including shoulder dystocia, death, and cesarean deliveries (2). Literature (3) also reports macrosomia in offspring of women with GDM, despite

documentation of maternal normoglycemia. Using continuous glucose sensors in women with GDM has shown that continuous monitoring detects postprandial glucose elevations not detected by intermittent fingerstick blood glucose determinations (4). Perhaps the previous notion “macrosomia despite normoglycemia” is in reality “macrosomia due to undetected hyperglycemia.”

Recent reports suggest that although postprandial hyperglycemia plays a major role in increasing the risk of macrosomia (1,4–7), it does not explain why the other 58% of the fetuses are not macrosomic. The “fidgety fetus hypothesis” seeks to explain this paradox, suggesting that fetal activity is an intrinsic trait that plays a role in determining subsequent birth weight. We hypothesize that some offspring of women with GDM may be intrinsically more active in utero, and those that are active may be able to compensate for the hyperglycemia and thus minimize their risk of macrosomia. We conducted a three-phase study to observe the relationship between fetal movements and subsequent birth weight of the fetus in women with diabetes. The first phase assessed fetal movements by maternal perception of fetal kicks. The second phase was designed to improve fetal monitoring techniques by home telemetry monitoring of fetal heart rate accelerations. The third phase applied our observations of fetal movements to a larger population of women with GDM who performed fetal heart rate (FHR) monitoring at clinic visits. This report describes all three phases and shows the relationship between fetal movement and subsequent birth weight.

## RESEARCH DESIGN AND METHODS

Subjects were recruited through the Santa Barbara County Health Services Diabetes Clinic after being diagnosed with GDM using the criteria from the Fourth International Diabetes Workshop-Conference (8) between 24 and 28 weeks of gestation. Insulin therapy was initiated if needed based on the workshop guidelines. Prepregnancy maternal weights were not included in the analysis because the subjects' medical records

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**Abbreviations:** FHR, fetal heart rate; GDM, gestational diabetes mellitus.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Table 1—Results of the neonatal birth weights from phases II and III

	Phase II			Phase III		
	Inactive*	Active†	P value‡	Inactive	Active	P value
Average birth weight (g)	3,530 ± 593	2,975 ± 570	0.04	3,629 ± 598	3,122 ± 553	0.0023
Average birth weight percentile corrected for gestational age (%)	63 ± 29	37 ± 22	0.05	62 ± 31	37 ± 24	0.0017

Data are means ± SD. \* $<4$  FHR accelerations/20 min. † $\geq 4$  FHR accelerations/20 min. ‡One-tailed distribution, two-sample unequal variance.

started at time of GDM diagnosis. All subjects signed informed consents approved by the Cottage Hospital Institutional Review Board. In phase I, 10 women with diabetes (mean age  $32 \pm 4$  years, HbA<sub>1c</sub> [A1C]  $5.5 \pm 0.6\%$ , normotensive, non-smokers, 7 with GDM, 2 with type 1 diabetes, and 1 with type 2 diabetes) were asked to perform fetal kick counts twice a day for 30 min and self-monitor their blood glucose before and 1 h after each meal. Subjects were instructed to schedule their monitoring sessions at the same time each day. The women were trained to detect gross fetal movements using fetal ultrasound for confirmation. The patients were asked to keep a diary documenting fetal movement and glucose values.

To improve our fetal monitoring techniques, in phase II, 13 women with GDM (mean age  $32 \pm 7$  years, A1C  $5.0 \pm 0.4\%$ , 8 treated on insulin and diet, and 5 controlled on diet alone) were recruited to test the feasibility of using a home fetal monitoring device. During session 1, the subjects were trained in the use of the Card Guard fetal monitor (CG-900P; Card Guard, Rehovot, Israel), which captures FHR, uterine contractions, and maternal perception of fetal movements. Previous studies report that the Card Guard fetal monitor has been easily and reliably operated by patients (9). Subjects performed a 20-min monitoring session daily at home for 4–6 weeks. Subjects were instructed to perform monitoring sessions at the same time everyday, between breakfast and lunch. The data were transmitted via modem and reviewed by a physician daily. FHR accelerations, defined as an increase in baseline fetal heart rate by at least 15 bpm sustained for at least 15 s, were employed as a surrogate marker to quantitate fetal activity since consistent linkage has been demonstrated between fetal body movements and FHR patterns (10,11). We chose to use a cutoff of FHR  $<4$  to define the inactive group based on the collected data from phase II. There was an obvious separation of the inactive and active groups at this level.

This definition was applied to both phases II and III (Table 1). An active fetus was defined as having  $\geq 4$  FHR accelerations in a 20-min period, and an inactive fetus was defined as having  $<4$  FHR accelerations in a 20-min period. All subjects adhered to a program of diet and self blood glucose monitoring (four or more times per day: fasting and 1 h postprandial). Insulin was initiated, and frequency of blood glucose monitoring increased to seven per day (fasting and preprandial and 1 h postprandial) if the fasting blood glucose was  $>90$  mg/dl and 1-h postprandial glucose concentrations were  $>120$  mg/dl.

In phase III, we applied our definitions of an active and inactive fetus to a larger population of 46 women with GDM (mean age  $32 \pm 6$  years, A1C  $5.4 \pm 0.5\%$ ) to examine the relationship between FHR accelerations and subsequent birth weight percentile, corrected for gestational age. We conducted a retrospective analysis of serial 20-min fetal monitoring strips (Hewlett-Packard HP 8041A) from women who visited the Santa Barbara County Health Services Diabetes Clinic between 9 and 11 AM. Each woman's total monitoring strips were then analyzed for FHR accelerations per 20 min. Characteristics of the patient population and infant outcome are listed in Table 2.

**RESULTS**— In all three phases of the study, there were no significant differences in the week that GDM was diag-

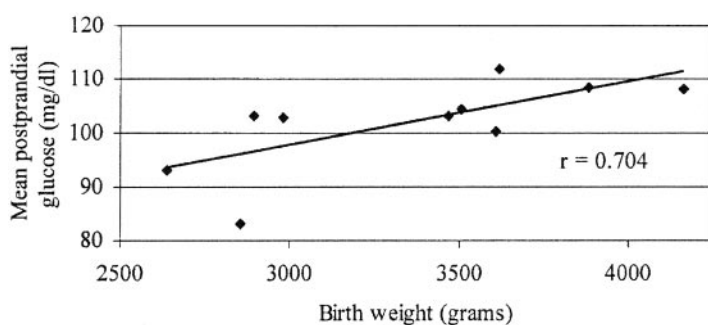
nosed, the week that insulin therapy was initiated, or the A1C levels between the inactive and active groups. In phase I, 71% of the recorded fetal movements and blood glucose records from the patients' diaries contained adequate assessment. Evaluation of the women's diaries showed little variability in fetal movements over a mean of 8.5 weeks (i.e., fetal kicks did not significantly deviate from one another on a day-to-day basis). There was no relationship between maternal weight and subsequent birth weight or the woman's ability to perceive fetal movements. Maternal postprandial glucose concentration ranged from 83 to 111 mg/dl with a mean of 102. Mean maternal postprandial glucose levels positively correlated with increased birth weight (Fig. 1;  $r = 0.704$ ). The ratio of 10 kicks per 1 mg/dl postprandial glucose value was calculated from the best correlation with birth weight. When the mean number of kicks per hour per day was divided by a factor of 10 and subtracted from the mean maternal 1-h postprandial glucose concentration, there was an improvement in the correlation between postprandial glucose and birth weight (Fig. 2;  $r = 0.773$ ). The relationship between the neonatal birth weight and the "adjusted maternal postprandial glucose level" continued to improve as the number of fetal movements per glucose concentration increased.

Placental weights and umbilical cord lengths were collected from seven of the participants. The infant that weighed the

Table 2—Characteristics of the patient population and infant outcome\*

	Phase I	Phase II	Phase III
n	10	13	46
Maternal age (years)	$32 \pm 4$	$32 \pm 7$	$32 \pm 6$
A1C (%)	$5.5 \pm 0.6$	$5.0 \pm 0.4$	$5.4 \pm 0.5$
Gestational age at delivery (weeks)	$39 \pm 0.9$	$37.8 \pm 1.7$	$38.5 \pm 1.7$
Birth weight (corrected for gestational age)			
Grams	$3,361 \pm 498$	$3,189 \pm 571$	$3,375 \pm 617$
Percentile	$53 \pm 35$	$49 \pm 37$	$54 \pm 40$

Data are means ± SD. \*There is no significant difference among the patient populations or infant outcome.



**Figure 1**—Phase I unadjusted mean postprandial glucose versus birth weight. ◆, each woman's unadjusted mean 1-h postprandial glucose value derived from the diaries.

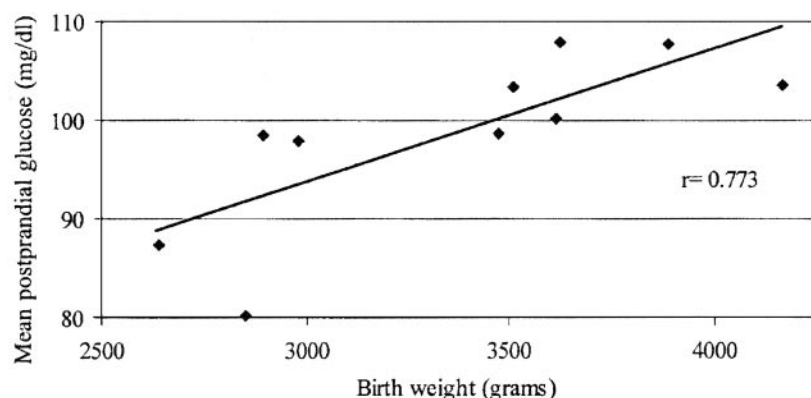
most also had the heaviest placenta and the longest cord length. There was a significant positive correlation between placental weight and birth weight ( $r = 0.798$ ,  $P = 0.032$ ) and placental weight and cord length ( $r = 0.912$ ,  $P = 0.004$ ).

In phase II, the fetal monitoring strips separated into two distinct groups determined to be "active" or "inactive," consistently illustrating that the active fetuses were always active and the inactive fetuses were always inactive. Mean birth weight percentile in the active group was 37 vs. 63% in the inactive group ( $P = 0.05$ ). This significant difference in birth weight percentile remained despite the fact that the mean maternal A1C levels were not significantly different in the two groups (5.1 vs. 4.9%, respectively,  $P = 0.47$ ).

In phase III, we observed an inverse correlation between the mean number of FHR accelerations and the birth weight percentile (Fig. 3). We found that the active fetus was more likely to be associated with a birth weight <50th percentile. In contrast, the inactive fetus was more likely to be associated with a birth weight >50th percentile. In addition, macro-

somic fetuses were only observed in the inactive group. The mean birth weight percentile in the active group was 37 vs. 62% in the inactive group ( $P = 0.0017$ ). This difference remained despite the fact that the mean maternal A1C levels were not significantly different in the two groups (5.3 vs. 5.4%, respectively,  $P = 0.92$ ) (Table 2).

**CONCLUSIONS**— The Fidgety Fetus Hypothesis suggests that fetal activity is a determinant of birth weight. Previous reports have examined the "fidget gene" in lean and obese adults and suggest that individual differences in activity level are biologically determined (12). Based on this notion, the Fidgety Fetus Hypothesis states that if physical activity is an intrinsic characteristic, then it should be expected to manifest itself in utero. If the fetus is overnourished by either intermittent or sustained maternal hyperglycemia, then those fetuses that are intrinsically active can minimize their risk of becoming macrosomic. Alternatively, those fetuses that are less active would be more affected by the hyperglycemia and



**Figure 2**—Phase I adjusted mean postprandial glucose versus birth weight. ◆, each woman's adjusted mean 1-h postprandial glucose value. Dividing the mean number of fetal kicks per day by a factor of 10 and subtracting the result from the mean maternal 1-h postprandial glucose concentration adjusted the glucose values from the patients' diaries.

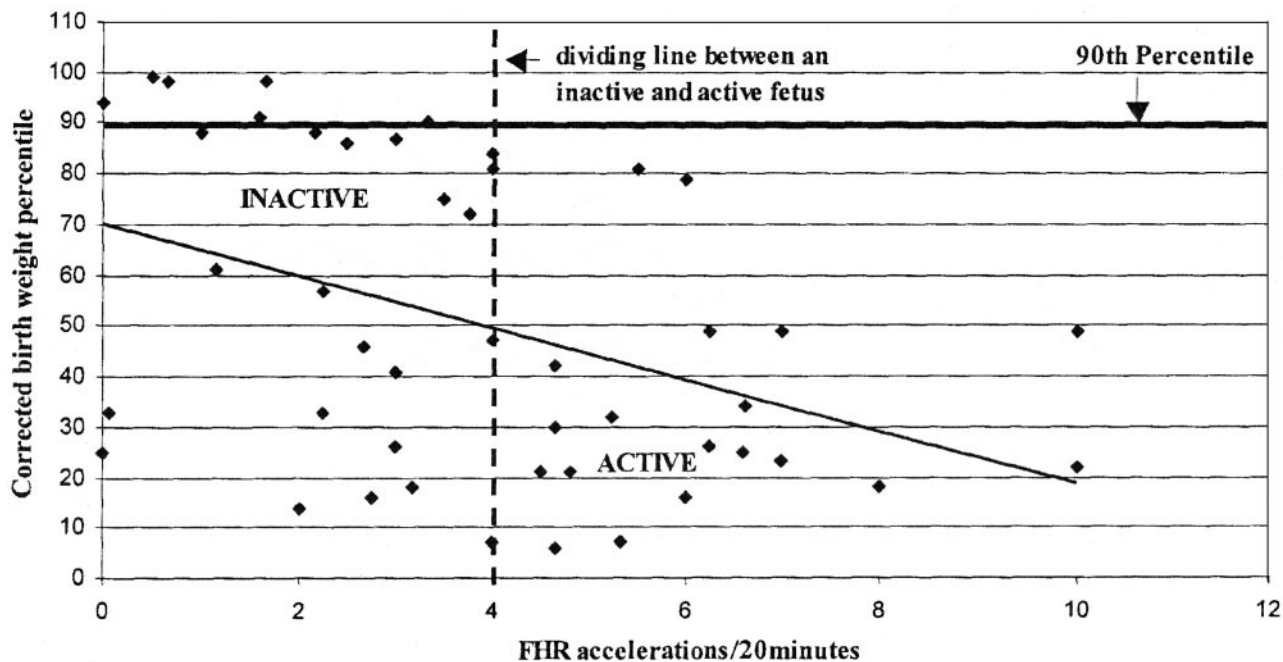
thus develop an increased likelihood of becoming macrosomic.

The pediatric literature (6,13–15) supports the Fidgety Fetus Hypothesis, lending insight into the fact that only 42% of the neonates born to women with diabetes are macrosomic, while the remaining 58% are not. The Framingham Children's Study found that low levels of activity during the preschool years had a moderately strong effect on increasing the child's level of adiposity during later childhood. The Bogalusa Heart Study and a literature review suggest that childhood obesity is related to both overnutrition and lack of physical activity, and the degree of physical activity seems to be intrinsic to each. The established factors that contribute to birth weight of the fetus are maternal age, race, genetics, and maternal/paternal physiognomy. Gestational diabetes, maternal obesity, parity, postpartum, and previous birth weights contribute to the development of macrosomia (16–19). We propose that fetal activity is an additional variable in determining birth weight.

The obstetric literature also supports the fidgety fetus hypothesis, claiming that fetal motor activity is an important factor in predicting neonatal motor activity (20,21). DiPietro et al. (20) discovered that fetal motor activity shows evidence of stability before birth and predicts aspects of temperament associated with regulatory control in early childhood. In addition, fetal motor activity was consistent with neonatal motor activity at 2 weeks, 4 weeks, and at 1 and 2 years. Thus, individual differences in motor activity level in the 1st month following birth were probably present during fetal life.

Froen (22) reinforced the importance of fetal movement counting as a method of screening for fetal well-being. His study determined that reduced fetal movements are associated with an adverse pregnancy outcome in both high- and low-risk pregnancies. He concluded that screening for fetal well-being by maternal fetal movement counting can reduce fetal mortality rates. Additionally, Pearson et al. (23) determined that 12-h fetal movement counts <10 (the lower limit of normal) were associated with fetal demise.

Previous short-term clamp studies (24–27) analyzing glucose extremes have shown a negative correlation between fetal movements and maternal glycemia. Fetal movements significantly increased with low maternal glycemia in pregnancies complicated by diabetes. Although



**Figure 3**—Corrected birth weight percentile versus FHR acceleration/20 min. ♦, birth weight percentile corrected for gestational age. INACTIVE and ACTIVE refers to the activity of the fetus. An inactive fetus has <4 FHR accelerations/20-min period and an active fetus has ≥4 FHR accelerations/20-min period. The dashed line represents the dividing line between an inactive and active fetus. The solid bold line represents a birth weight in the 90th percentile.

maternal hyperglycemia was associated with low fetal movement counts, this may have been associated with a sick fetus.

Our three-phased study has shown that intrinsic fetal activity minimizes the impact of maternal hyperglycemia and puts the fetus at a decreased risk of becoming macrosomic. In phase I, although we confirmed that both placental weight and cord length relate positively to birth weight, our new observation was that the more active the fetus was, in spite of postprandial hyperglycemia, the less likely he or she was large for gestational age. In phase II, this observation was confirmed by home fetal telemetric monitoring. In addition, phase III of our study confirmed that glucose-mediated macrosomia was only present in the inactive fetus group.

In summary, the fetus appears to play a role in determining its own destiny. Increased fetal activity, as a response to increased maternal glucose or as an intrinsic trait, can negate the impact of maternal hyperglycemia on birth weight. The inactive fetus appears to be at a higher risk for glucose-mediated macrosomia. Although normoglycemia is the goal of therapy in all women with diabetes, in those women whose fetuses manifest less movement, increased surveillance and treatment of hyperglycemia is of utmost importance. Perhaps an indicator of fetal movement

could be combined with indicators of maternal glycemia to improve the ability of predicting birth weight in pregnancies complicated by diabetes.

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