Long-Term Impact of Neonatal Breast-Feeding on Body Weight and Glucose Tolerance in Children of Diabetic Mothers

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OBJECTIVE — Offspring born to women with pregnancies complicated by diabetes are at increased childhood risk of developing obesity and impaired glucose tolerance (IGT). In population-based studies, breast-feeding has been shown to be protective against obesity and diabetes later in life. To date, the role of breast-feeding on offspring of diabetic mothers (ODM) has not been investigated in this context.

RESEARCH DESIGN AND METHODS — A total of 112 ODM (type 1 diabetes, $n = 83$; gestational diabetes, $n = 29$) were evaluated prospectively for impact of ingestion of either diabetic breast milk (DBM) or nondiabetic banked donor breast milk (BBM) during the early neonatal period (day 1–7 of life) on relative body weight and glucose tolerance at a mean age of 2 years.

RESULTS — There was a positive correlation between the volume of DBM ingested and risk of overweight at 2 years of age (odds ratio [OR] 2.47, 95% CI 1.25–4.87). In contrast, the volume of BBM ingested was inversely correlated to body weight at follow-up ($P = 0.001$). Risk of childhood IGT decreased by increasing amounts of BBM ingested neonatally (OR 0.19, 95% CI 0.05–0.70). Stepwise regression analysis showed volume of DBM to be the only significant predictor of relative body weight at 2 years of age ($P = 0.001$).

CONCLUSIONS — Early neonatal ingestion of breast milk from diabetic mothers may increase risk of becoming overweight and, consequently, developing IGT during childhood. Additional studies are needed to assess long-term consequences that might result from the type of neonatal nutrition in ODM.

Diabetes Care 25:16–22, 2002

In population-based studies, breast-feeding has been shown to be protective against obesity and diabetes later in life (1–6). This effect was attributed to the difference in composition of formula milk as compared with breast milk, which resulted in early postnatal overnutrition of formula-fed infants (4). Offspring of diabetic mothers (ODM) are at increased risk of developing obesity and impaired glucose tolerance (IGT) beginning early during childhood (7–11). The mechanisms responsible are not completely understood. Data from clinical (8,10,11) and experimental studies in animal models (12–14) have shown that a diabetic intrauterine environment plays a key role in fetal programming for increased susceptibility to obesity and diabetes. The role of breast-feeding in ODM has not been investigated to date, but if a similar protective effect as in normal populations exists, it would potentially be of great benefit. However, diseases of the mother considerably influence the composition of breast milk. In some studies, energy content and macronutrient composition of breast milk from women with diabetes were characterized (15). Increased concentrations of glucose and insulin as well as a higher energy content of diabetic breast milk were observed, as compared with breast milk from healthy mothers (16,17). Even in diabetic mothers with good metabolic control, considerable alterations were found in colostrum and transitional milk (18,19). Remarkably, in utero exposure to increased concentrations of glucose and insulin is followed by an increased risk for obesity and insulin resistance later in life (8,10,11). It has been speculated that even a small increase in energy intake resulting from alterations of diabetic breast milk might have long-term consequences for body weight and metabolism in breast-fed ODM (17).

Until now, no studies have characterized the influence of neonatal nutrition on the development of body weight and glucose tolerance in ODM. Moreover, there has been, in general, no study of the possible long-term consequences of any noncommunicable maternal disease during breast-feeding on later outcome of the offspring. Because altered composition and energy content were shown to be particularly pronounced in colostrum and transitional milk of diabetic mothers (18,19), our study focused on the consequences of diabetic breast-feeding during the early neonatal period.

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Received for publication 23 July 2001 and accepted in revised form 25 September 2001.

Abbreviations: BBM, nondiabetic banked donor breast milk; DBM, diabetic breast milk; GDM, gestational diabetes; IGT, impaired glucose tolerance; ODM, offspring of diabetic mothers; OGTT, oral glucose tolerance test; OR, odds ratio.

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

RESEARCH DESIGN AND METHODS

Participants

During the study period (1980–1989), 368 ODM were delivered at the Clinic of Obstetrics and Gynecology, Berlin-Kaulsdorf, Berlin (former East Germany). Each mother was offered the opportunity to have her child participate in pediatric follow-up with regular physical reexaminations, which included an oral glucose tolerance test (OGTT). A total of 112 infants were brought for follow-up; complete data on nutrition during the early neonatal period (day 1–7 of life) was available for all of the infants.

Pregnancy data

Maternal demographic data included age, duration of diabetes (type 1), and maternal prepregnancy BMI. Socioeconomic status was categorized by maternal (or paternal) occupation: unemployed (mother, $n = 2$; father, $n = 0$), manual worker (mother, $n = 20$; father, $n = 79$), nonmanual worker without high school diploma (mother, $n = 71$; father, $n = 22$), and nonmanual worker with high school diploma (mother, $n = 19$; father, $n = 11$). Geographic origin was defined as urban ($n = 76$) or rural ($n = 36$). Gestational age and birth weight were taken from birth records.

Gestational diabetes (GDM) was diagnosed between the 26th and 28th weeks of gestation using a 50-g OGTT, as described in detail previously (10,11,20). After diagnosis of GDM, glucose homeostasis was monitored weekly by 24-h day-night glucose profiles at the clinic. During monitoring, blood samples were measured every 2 h using the glucosidase-peroxidase method. Women maintaining mean 24-h profiles <5.5 mmol/l were treated with diet therapy ($n = 14$). When a woman's mean profile was ≥5.5 mmol/l, insulin therapy was initiated ($n = 15$). After insulin therapy was started in women with GDM, glycemic monitoring was instituted and insulin therapy was titrated in these women, as in women with type 1 diabetes, to achieve euglycemia (20).

Infant nutrition during first week of life

After delivery, all mothers stayed with their newborns at the maternity ward of the clinic for at least 1 week. All were encouraged to breast-feed their newborns. Depending on the status of maternal lactation, when necessary (as judged by the pediatrician at the ward) a supplementary feeding with banked donor breast milk was offered to the neonate. Donor breast milk was provided by the local center for donation of breast milk at the Clinic of Pediatrics Lindenhof, Berlin, East Germany. Women with diabetes were excluded from donating breast milk; therefore, all banked breast milk was nondiabetic milk. Thereby, all newborns in the study received differing amounts of breast milk from their biological diabetic mothers and banked donor breast milk from unrelated nondiabetic women. Because of acute nonavailability of banked breast milk, in 23 infants, short-time supplementation was necessary with standard term formula milk (Milasan; Milchwerke Stendal, Stendal, East Germany). The mean nutrient contents per 100 ml of the formula milk were 3.8 g fat, 1.9 g protein, and 6.2 g carbohydrate, including 4.9 g lactose; energy content per 100 ml was 282 kJ.

During each feeding on days 1–7 postpartum, milk intake was determined using a test weighing protocol (4,21): the infant was weighed before and after every nursing by trained staff. The weight difference (in g) and the type of milk ingested during the meal was noted as breast milk from the biological (diabetic) mother (diabetic breast milk [DBM]), banked donor breast milk from unrelated nondiabetic mothers (nondiabetic banked donor breast milk [BBM]), or standard term formula milk. Mean volume of milk ingested per day (g/day) was calculated for each type of milk separately by summing the volumes ingested during the period (days 1–7 postpartum) and dividing by 7. Because formula milk was given to only 23 infants, a number too small for allowing valid statistical evaluation, further analysis was restricted to the impact of DBM and BBM feeding.

Anthropometry at follow-up

During follow-up examinations, at a median age of 2 years, body weight and height were recorded. From these data, relative body weight was calculated for all children in relation to age- and sex-specific standard population measures (rounded to year) as follows: relative weight (individual weight divided by median standard weight for age and sex) divided by relative height (individual height divided by median standard height for age and sex) × 100 (7,8,10). The resulting relative body weight percentage allowed the combination of data obtained in male and female children (6–8,10). Standards for median weight and height according to age and sex were obtained from Flügel et al. (22) and determined from cross-sectional studies conducted between 1979 and 1982 in East Germany (38,000 boys, 35,000 girls). Relative body weight >110% was defined as overweight (10,23,24).

OGTT at follow-up

At 2 years of age, OGTTs were performed in the morning after a 12-h overnight fast. During the test, children remained prone, resting in bed. Capillary blood samples were collected in the fasting state and then 120 min after ingesting an oral glucose load of 1.75 g glucose/kg body wt in a 40% glucose solution. Blood glucose concentration was determined using the glucosidase-peroxidase method. Impaired glucose tolerance (IGT) was defined according to the National Diabetes Data group criteria recommended for children: fasting glucose in capillary whole blood <6.7 mmol/l and 120-min glucose concentration >6.7 mmol/l (25).

In all cases, informed consent for data evaluation was given. All procedures were in accordance with the local ethical standards and with the Helsinki Declaration of 1975, as revised in 1983.

Statistical analysis

Data are expressed as means ± SEM and n. To analyze relationships between the volume of different types of milk consumed neonatally and later outcome (relative body weight and glucose tolerance), the mean volume of DBM and BBM consumed during the first 7 days of life were divided into tertiles. Differences between tertiles were analyzed using one-way analysis of variance (followed by post hoc Student's t test) and χ^2 statistics. For analysis of relationships between continuous variables, univariate linear regression analysis was performed. To estimate the risk for becoming overweight and developing IGT in relation to the volume of different types of milk consumed neonatally, the odds ratio (OR) with 95% CI were calculated using logistic regression analysis. Stepwise regression analysis was used to estimate the relative impact of dif-

Table 1—*Population characteristics of diabetic mothers (type 1 diabetes; GDM) and their offspring at birth and at follow-up*

	Type 1 diabetes (n = 83)	GDM (n = 29)	P*
Maternal parameters			
Maternal age (years)	25 ± 0.61	26 ± 1.0	0.17
Maternal BMI (kg/m^2)	25 ± 0.49	25 ± 1.1	0.86
Pregestational duration of diabetes (years)	9.6 ± 0.62	NA	—
Gestational age (weeks)	38 ± 0.14	39 ± 0.27	0.11
Neonatal parameters			
Birth weight (kg)	3,440 ± 74	3,372 ± 78	0.61
Mean daily milk intake (days 1–7 of life)			
DBM (g/day)	85 ± 7.1	112 ± 12	0.05
BBM (g/day)	37 ± 4.1	21 ± 6.6	0.05
Follow-up at 2 years of life			
Mean age	2.0 ± 0.12	2.4 ± 0.21	0.08
Relative body weight (%)	104 ± 1.5	105 ± 2.3	0.67
Overweight	24 (20/83)	34 (10/29)	0.33
Blood glucose during OGTT			
Fasting (mmol/l)	4.3 ± 0.07	4.4 ± 0.11	0.67
120 min (mmol/l)	5.2 ± 0.09	5.4 ± 0.22	0.32
Impaired glucose tolerance	8.4 (7/83)	14 (4/29)	0.47

Data are means ± SEM or % (n). *Type 1 diabetes versus GDM (unpaired Student's t test or χ^2 test).

ferent independent variables on outcome variables. For all evaluations, $P < 0.05$ was considered significant. All statistical tests were accomplished using the SPSS for Windows version 9.0 statistical software package (SPSS, Munich, Germany).

RESULTS — Of the 112 children studied, 83 were born to women with type 1 diabetes and 29 were born to women with GDM. The mean age at time of follow-up was 2.1 ± 0.1 years. In women with type 1 diabetes, the mean duration of diabetes before pregnancy was 9.6 ± 0.6 years. Macrosomia (birth weight >4,500 g) occurred in 6% (5 of 83) of infants of mothers with type 1 diabetes and in none of the newborns of women with GDM. Study population characteristics are shown in Table 1.

As shown in Table 2, mean relative body weight during childhood differed significantly by tertiles of DBM volume ingested neonatally. Infants in the highest tertile of intake of breast milk from their biological (diabetic) mother had a higher relative body weight at 2 years of age, as compared with those in the first tertile ($P = 0.001$) (Fig. 1).

This resulted in a significantly higher prevalence of overweight children in the third tertile of distribution of DBM, as compared with those in the first tertile ($P = 0.03$). There was no significant relationship between the tertile of neonatal DBM intake and fasting or 2-h blood glucose concentration, or the prevalence of IGT in childhood.

Conversely, the volume of BBM ingested during neonatal life was inversely related to relative body weight at follow-up (Table 3): Infants in the third tertile of distribution of BBM had a lower body weight, as compared with those in the first tertile ($P = 0.004$). The rate of overweight children and mean blood glucose concentration at 0 and 120 min during OGTT in childhood did not differ significantly between tertiles of BBM distribution. Infants in the second and third tertile of neonatal BBM intake distribution had, however, a lower prevalence of IGT, as compared with those in the first tertile ($P = 0.03$, $P = 0.04$).

Univariate linear regression analysis showed that the volume of DBM ingested during the first week of life was positively correlated with relative body weight during infancy ($P < 0.001$) (Table 4). Conversely, volume of BBM ingested neonatally was inversely correlated with relative body weight in childhood ($P = 0.001$). By logistic regression analysis, risk for overweight at 2 years of age was significantly higher in children in the third versus first tertiles of DBM intake distribution (OR 1.91, 95% CI 1.10–3.30). Increased risk for overweight in infants who received more DBM during neonatal life was still observed after adjusting for birth weight, gestational age, sex, age, type of maternal diabetes, and maternal BMI (OR 2.59, 95% CI 1.32–5.04).

By univariate linear regression analysis, volume of DBM ingested during the first week of life was positively correlated with blood glucose concentration at 120 min during OGTT ($P = 0.03$) (Table 4). Conversely, volume of BBM ingested neonatally was inversely correlated with blood glucose concentration at 120 min during OGTT ($P = 0.02$). Relative body weight during childhood was positively correlated with 120-min blood glucose concentration during OGTT ($P = 0.01$). By logistic regression analysis, risk for IGT at 2 years of age was significantly decreased in children in the third tertile of BBM intake distribution, as compared with the first tertile (OR 0.27, 95% CI 0.10–0.77). Again, adjustment for the

Table 2—*Relative body weight, prevalence of overweight, blood glucose concentration at fasting and at 120 min during OGTT, and prevalence of IGT at 2 years of age (mean 2.1 ± 0.1 years) according to the tertiles of mean daily consumption of DBM during the first 7 days of life*

	Tertiles of DBM volume (g/d)			
Parameter at 2 years of age	First (≤56)	Second (57–124)	Third (≥125)	Significance (P)*
Relative body weight (%)	98 ± 1.7	104 ± 1.8	109 ± 2.8†	0.002
Overweight (n)	5/37	11/38	14/37‡	0.05
Fasting blood glucose level (mmol/l)	4.3 ± 0.12	4.3 ± 0.09	4.5 ± 0.11	0.13
120-min blood glucose level (mmol/l)	5.0 ± 0.17	5.3 ± 0.14	5.5 ± 0.16	0.13
IGT (n)	4/37	3/38	4/37	0.89

Data are means ± SEM or n. *By analysis of variance or χ^2 test for trend; †$P = 0.001$ versus first tertile (post-hoc Student's t test); ‡$P = 0.03$ versus first tertile (χ^2 test).

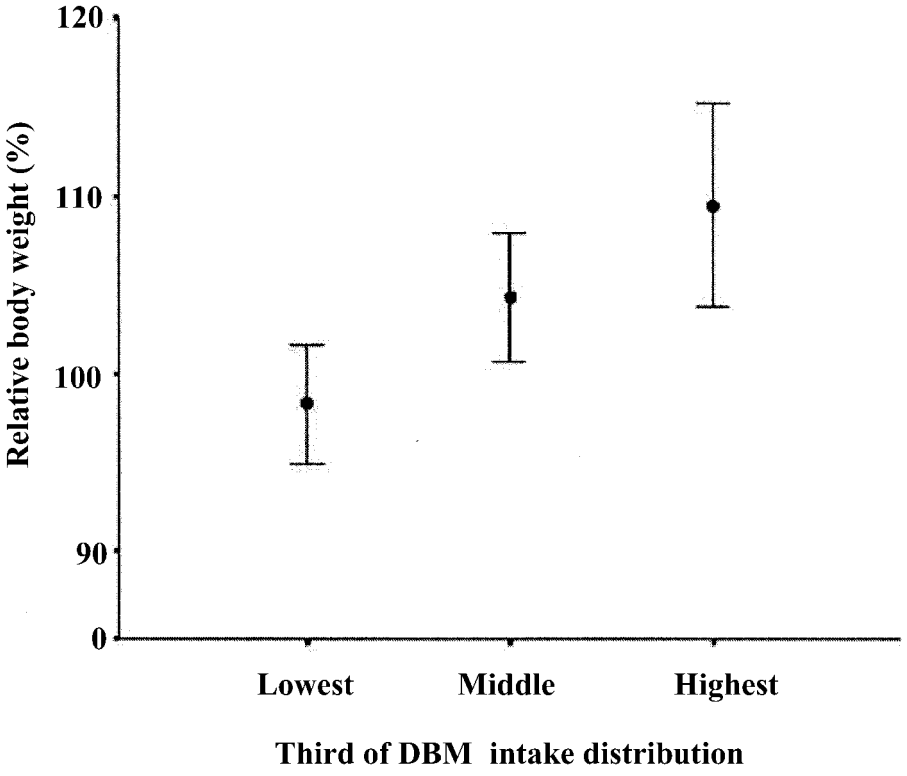

Figure 1—*Relative body weight at 2 years of age in thirds of intake of DBM (error bars = 95% CI).*

confounders, plus additional adjustment for relative body weight at follow-up, did not change this result (OR 0.18, 95% CI 0.05–0.68).

Finally, to analyze the independent influence of neonatal nutrition on body weight and glucose tolerance in childhood, stepwise regression models were developed using relative body weight and blood glucose concentration at 120 min during OGTT in childhood as dependent variables. Birth weight, gestational age, sex, age, type of maternal diabetes, maternal BMI, volume of DBM, and volume of BBM were entered as independent variables into a stepwise regression analysis with relative body weight during childhood as the dependent variable. As shown in Table 5, the volume of DBM ingested neonatally was the only significant predictor of relative body weight during childhood, whereas all other variables did not improve the fit. In a second stepwise regression model, blood glucose concentration at 120 min during OGTT was used as a dependent variable. Birth weight, gestational age, sex, age, type of maternal diabetes, maternal BMI, volume of DBM, volume of BBM, and relative body weight during childhood served as independent variables. Table 5 shows that, by stepwise regression analysis, relative body weight at follow-up was the only significant predictor of 120 min blood glucose concentration at 2 years of age.

CONCLUSIONS — In summary, the results of our study indicate that in children of mothers with diabetes during pregnancy, the early neonatal ingestion of breast milk provided by their biological (diabetic) mother may result in an increased relative body weight and increased prevalence of obesity at 2 years of age, independent of birth weight, gestational age, sex, age, type of maternal diabetes, or maternal BMI. In contrast, neonatal intake of banked breast milk from healthy nondiabetic women has a beneficial effect on later body weight and glucose tolerance in childhood. Although the volume of diabetic breast milk ingested neonatally significantly predicted relative body weight at 2 years of age, body weight itself was the only significant predictor of glucose tolerance at follow-up, as revealed by stepwise regression analysis.

To our knowledge, only one study has investigated the impact of the amount of certain types of milk ingested neonatally on later outcome, in general. Singhal et al. (26) observed a beneficial effect of the amount of banked donor breast milk ingested during neonatal life, as compared with formula milk, on blood pressure later in the childhood of preterm newborns. In a number of studies, decreased body weight, diminished risk for obesity, and decreased risk for development of type 2 diabetes were observed in breast-fed infants (1–6). Moreover, by analyzing potential influences of a wide range of social and economic factors, as well as those of nutrition during later infancy, lasting effects from the type of neonatal nutrition were described in a large study sample (5). However, all these studies were performed in healthy (i.e., nondiabetic) women and their infants. We could confirm here a protective effect of feeding breast milk from healthy mothers

Table 3—*Relative body weight, prevalence of overweight, blood glucose concentration at fasting and at 120 min during OGTT, and prevalence of IGT at 2 years of age (mean 2.1 ± 0.1 years) according to the tertiles of mean daily consumption of BBM during the first 7 days of life*

	Tertiles of BBM volume (g/day)			
Parameter at 2 years of age	First (≤11)	Second (12–37)	Third (≥38)	Significance (*P*)*
Relative body weight (%)	109 ± 2.8	104 ± 1.8	99 ± 1.8†	0.005
Overweight (*n*)	12/37	11/38	7/37	0.39
Fasting blood glucose level (mmol/l)	4.3 ± 0.11	4.5 ± 0.09	4.3 ± 0.12	0.60
120-min blood glucose level (mmol/l)	5.4 ± 0.17	5.3 ± 0.14	5.0 ± 0.15	0.17
IGT (*n*)	8/37	2/38‡	1/37§	0.01

*By analysis of variance or χ^2 test for trend; †$P = 0.004$ versus first tertile (post hoc Student's *t* test); ‡$P = 0.04$ versus first tertile (χ^2 test); §$P = 0.03$ versus first tertile (χ^2 test).

Table 4—*Univariate linear regression analysis of factors predicting relative body weight and blood glucose concentration at 120 min during OGTT at 2-year follow-up*

Predictors	β	*P*
Relative body weight at 2 years		
DBM volume	0.33	<0.001
BBM volume	−0.30	0.001
120-Min blood glucose concentration at 2 years		
DBM volume	0.20	0.03
BBM volume	−0.21	0.02
Relative body weight at 2 years	0.24	0.01

on later risk to become overweight and to develop IGT by a negative correlation between the volume of BBM ingested neonatally and body weight and glucose tolerance during childhood. Unfortunately, no data were available on nondiabetic control subjects followed in the same way to verify that, in this population, breast-feeding was associated with reduced risk for obesity.

Until now, only one study reflected a possible long-term influence of breast-feeding in diabetic women for the development of glucose tolerance in offspring. In the Pima Indian population, a beneficial effect of breast milk was suggested; however, no distinct data analysis was provided (27). In our study, we found an unexpected strong positive correlation between the neonatal intake of diabetic breast milk and later body weight. By adjusting for a variety of maternal and infant confounders, such as type of maternal diabetes, birth weight, gestational age, and maternal BMI, we were unable to detect any other main factor that could contribute to this relationship. Moreover, our data indicate that long-term effects of the type of early nutrition affect offspring of GDM mothers as much as offspring of type 1 diabetic mothers. For determination of milk intake, we used a weighing procedure, as developed by other investigators (4,21). Values we obtained are in good agreement with those reported in another study on milk intake of offspring of diabetic mothers (28), further supporting the validity of our data.

The question arises regarding what biological mechanisms, or what component of breast milk, could be responsible for the relationship between neonatal intake of diabetic breast milk and increased body weight in childhood. As already pointed out, some studies show that breast milk from diabetic women has an increased energy content (15). Furthermore, because glucose concentrations in breast milk were shown to follow the concentration of blood glucose proportionally (17,29), increased milk glucose concentrations can be expected to occur in type 1 diabetic women and also in mothers with GDM, who usually do not show complete normalization of glucose metabolism immediately after pregnancy (30,31). Indeed, breast milk of diabetic women was reported to be characterized by increased glucose concentrations, particularly when colostrum was analyzed (16,18,19). Furthermore, breast milk from diabetic mothers was shown to contain several-fold increased concentrations of insulin (17), which is able to cross the intestinal mucose-blood barrier during neonatal life (32). Therefore, it is possible that early in neonatal life, increased levels of intact insulin are absorbed from the breast milk of diabetic mothers. Drinking a glucose- and insulin-laden milk so early in life might, therefore, promote accelerated weight gain. However, pathophysiological mechanisms remain to be established. However, a number of studies suggest that in utero exposure to increased concentrations of glucose and insulin leads to an increased risk of developing obesity and insulin resistance later in life (8,10,11). Most recently, Singhal et al. (26) speculated that trophic factors and hormones occurring in breast milk might be responsible for the long-term effects of breast-feeding found in several studies (1–6).

To our knowledge, this study is the first one describing lasting effects of the *volumes* of different types of milk ingested during the first week of life on later development in humans. In animals, effects of colostrum feeding, even during the first few hours of postnatal life, were reported on a variety of parameters (33,34). More

Table 5—*Stepwise regression analysis of factors predicting relative body weight and blood glucose concentration at 120 min during OGTT at 2-year follow-up*

Predictors	β	*P*
Relative body weight		
Included		
DBM volume	0.33	0.0001
Excluded		
Birth weight	0.15	0.09
Gestational age	−0.001	0.99
Sex	0.03	0.76
Age at reexamination	−0.02	0.86
BBM volume	−0.19	0.06
Type of maternal diabetes	−0.02	0.80
Maternal BMI	0.03	0.75
Blood glucose concentration at 120 min		
Included		
Relative body weight	0.24	0.012
Excluded		
Birth weight	0.03	0.73
Gestational age	−0.01	0.87
Sex	0.02	0.79
Age at reexamination	−0.07	0.42
DBM volume	0.14	0.16
BBM volume	−0.16	0.11
Type of maternal diabetes	0.08	0.36
Maternal BMI	0.05	0.58

specifically, a number of animal studies support the hypothesis that early neonatal nutrition "programs" the later development of body weight and glucose metabolism, e.g., artificial reduction of the number of suckling pups in lactating rats ("small litters") leads to increased energy content and glucose concentrations in the dam' s milk (35). During later life, rats raised in small litters display persisting obesity and impaired glucose tolerance (36,37). Moreover, early postnatal overnutrition was shown to enhance a preexisting genetic disposition, thereby leading to the development of infantile obesity (38). Recently, it was shown that in backcrossed New Zealand Obese mice, a "genetic" animal model for type 2 diabetes, the occurrence of obesity and diabetic metabolic alterations is partly explained by neonatal ingestion of milk from their biological (diabetic) mothers and can be prevented, at least in part, by cross-fostering the offspring on nondiabetic dams (39).

Currently, diabetic women are encouraged and choose to breast-feed their newborns as often as healthy women do (40). Our findings, assuming that they can be extrapolated to other populations, might offer a dilemma to women with diabetes and their babies. Therefore, before any practical conclusions should be drawn, additional studies on the long-term consequences of the type of neonatal nutrition in offspring of diabetic mothers are needed. Meanwhile, considering the variety of advantages resulting from breast-feeding in general, in our opinion, breast-feeding should remain the preferred type of infant feeding, even in this particular population. Furthermore, in most parts of the world, banked breast milk will not be readily available and, therefore, would not offer an alternative neonatal nutrition in offspring of diabetic mothers. Consequently, future studies including data evaluation on effects of formula milk will be necessary to judge what kind of neonatal nutrition might offer a safe and practical alternative for offspring of diabetic mothers. Finally, a study of banked breast milk versus commercial milk among offspring of both diabetic and nondiabetic women is suggested to determine whether it is consumption of milk from bottle per se that leads to obesity or if banked breast milk is truly less fattening.

In conclusion, because diabetes during pregnancy is increasingly realized to be a major health problem, affecting a large and continuously increasing number of pregnant women, our data underscore the urgent need for additional studies of this important at-risk population to assess long-term consequences from the type of neonatal nutrition. Thereby, new approaches for genuine prevention of lasting adverse effects on the health outcome in offspring of diabetic mothers may be achieved.

Acknowledgments— This study was supported by the German Diabetes Association (DDG) and by the German Research Foundation (DFG, PL 241–1/3).

We thank Siri L. Kjos, MD, for helpful comments and linguistic revision of the manuscript.

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