

Dietary Composition of Pregnant Women Is Related to Size of the Baby at Birth^{1,2}

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ABSTRACT The fetal origins theory of adult disease suggests that term infants who are small for their gestational age have an increased susceptibility to chronic disease in adulthood as a consequence of physiologic adaptations to undernutrition during fetal life. Consistent evidence for an influence of women's dietary composition during pregnancy on growth of their babies is lacking, despite robust effects in animal experiments. We undertook a prospective observational study of 557 women aged 18–41 y, living in Adelaide, South Australia. Diet was assessed in early and late pregnancy using an FFQ. In early pregnancy, medians for energy intake, the proportion of energy derived from protein and from carbohydrate were 9.0 MJ, 17 and 48%, respectively. In late pregnancy the corresponding medians were 9.2 MJ, 16 and 49%. In early pregnancy, the percentage of energy derived from protein was positively associated with birth weight ($P = 0.02$) and placental weight ($P = 0.07$), independently of energy intake and weight gain during pregnancy, and after adjustment for potential confounders, including maternal age, parity, and smoking. Effects were stronger among women ($n = 429$) who had reliable data, based on prespecified criteria including the plausibility of dietary data when referenced against estimated energy expenditure. In addition, for this subgroup, the percentage of energy from carbohydrate in early and late pregnancy was negatively associated with ponderal index of the baby, and a specific effect of protein from dairy sources was identified. These data support the proposition that maternal dietary composition has an effect on fetal growth. Maternal diet in Western societies may therefore be important for the long-term health of the child. *J. Nutr.* 134: 1820–1826, 2004.

KEY WORDS: • pregnancy • dietary composition • fetal growth • birth weight

In Western societies, nutrition of women during pregnancy is widely regarded as important for the development of the unborn baby, despite a lack of strongly supportive evidence. The quality of the diet, rather than its quantity, appears to be a common concern (1).

Two distinct adverse outcomes of pregnancy are shortened gestation and restricted fetal growth (2). Shortened gestation may not be related to nutritional factors. However, the most important established determinants of restricted fetal growth in Western settings, after cigarette smoking, are low prepregnancy BMI and low gestational weight gain (3). These 2 anthropometric factors primarily reflect inadequate food intake, which might be due to extreme poverty or to the cultural desirability of being thin.

Some researchers, such as Rosso (4), maintain that in the absence of specific micronutrient deficiencies, effects of maternal diet on fetal growth will occur only when women have low prepregnancy BMI or their energy intake does not meet their energy needs during pregnancy. However, it is possible that the sources of dietary energy may influence fetal growth, through accompanying micronutrients and effects on their bioavailability, or because the proportion of nutrients directed to the fetus may depend on dietary composition (5).

Renewed interest in nutrition during pregnancy has been generated by the fetal origins theory of adult disease (6). This theory suggests that term infants who are small for their gestational age have an increased susceptibility to cardiovascular disease and Type II diabetes in adulthood as a consequence of physiologic adaptations to undernutrition during fetal life. The epidemiologic studies linking size at birth to disease in adulthood have highlighted the informativeness of placental weight and thinness at birth, indicated by ponderal index, as markers of fetal growth in addition to weight for gestational age.

Animal experiments prompted by the fetal origins theory clearly show that variations in maternal nutrition during pregnancy can induce permanent changes in the structure of tissues and organs and in physiologic functioning of the off-

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spring (7). The animal research has focused primarily on 2 dietary manipulations, a reduction in total energy and an isoenergetic low protein diet.

In a recent editorial, Barker (8) identified the macronutrient balance in maternal diets as 1 of 2 important themes emerging from the Second World Congress on the Fetal Origins of Adult Disease. Although there have been several recent investigations of maternal dietary composition and birth size in Western settings (9–12), there are inconsistencies in results. We therefore undertook a prospective study to assess relations between a woman's macronutrient intakes in early and late pregnancy and the weight of the placenta as well as weight and thinness of the baby at birth. We hypothesized that the protein content of the maternal diet would be positively associated with the size of the baby and placenta at birth (independently of energy intake and weight gain during pregnancy), whereas the carbohydrate content would be negatively associated with birth characteristics.

SUBJECTS AND METHODS

Participants. We undertook a prospective observational study of pregnant women living in Adelaide, South Australia. Women were identified through the antenatal clinic at a public hospital and through the offices of 3 privately practicing obstetricians. At the hospital, women attending the antenatal clinic on specified days were approached, with the clinic days rotated following a random schedule. At the private practices, where the client numbers were much smaller, all eligible women were approached. Our aim was for half of the study participants to be drawn from the hospital setting because that is about the proportion of South Australian women who receive antenatal care in a hospital clinic (13).

To be eligible to take part in the study a woman had to meet the following criteria: 1) Caucasian and aged at least 18 y old; 2) in the first 16 wk of a singleton pregnancy in which conception occurred without treatment for infertility; 3) planning to give birth in 1 of the 5 hospitals cooperating in the study; 4) not diabetic; 5) sufficiently fluent in English for completion of study questionnaires and able to give informed consent. Ethics approval was obtained from all hospitals cooperating in the study. Written consent was obtained from all participating women.

Data collection. Women were interviewed on 2 occasions, before 16 complete weeks of pregnancy and between wk 30 and 34 of pregnancy. During each interview, information concerning the pregnancy, medical history, and social circumstances was sought. Height was measured at the first interview, using a stadiometer, and weight was measured at both interviews using digital scales. During each interview, a dietary assessment was completed, as described below.

We arranged for midwifery staff to measure each baby at birth and weigh the placenta, after removing clotted blood and trimming the cord at the base. Further data about the course of pregnancy, including complications, were abstracted from hospital records. Duration of gestation was determined from the date of the last menstrual period, unless this was unknown or differed by more than 7 d from the date based on an ultrasound scan in early pregnancy. Discrepant cases were reviewed; when there were no errors or documented explanation, the ultrasound date was used.

Dietary assessment. The dietary assessment was carried out in a face-to-face interview, using a semiquantitative FFQ covering almost 200 food items, with photographs of reference meals to assist in determining serving sizes. This method was chosen to maximize the participation rate of women in disadvantaged circumstances and was modeled on the European Prospective Investigation of Cancer (14). Information on supplements was also obtained, although it was not used in the present analyses.

We compared the relative validity of the FFQ and 4-d weighed food records (WFR) for 24 women in the first trimester of pregnancy. The same food tables (Australian Food Composition Tables, NUTAB91–92) (15) were used to generate estimates of daily intakes of total energy, the energy sources that were the exposures of interest (protein, fat, and carbohydrate), and micronutrients for which a

limited number of days of diet records provides satisfactory ranking of individuals (calcium, magnesium, and potassium) (16).

Two models for estimating intakes from the FFQ, which differed in the assumptions underlying the intakes of infrequently consumed items, were assessed against the WFR. In 1 model, items consumed "1 to 3 times per month" and "less than once per month" were assigned consumption frequencies of 2 times/mo and 6 times/y, respectively. In the second model the corresponding frequencies were reduced to 1.5 times/mo and 3 times/y. For both models, Spearman's correlation coefficients were between 0.5 and 0.7, >46% of participants were correctly classified and <8% grossly misclassified into thirds, and weighted κ values were >0.4 as recommended by Masson et al. (17). Using the second model, mean values were closer to those obtained by the WFR (within 2%) than when using the first model. We therefore chose to use the second model to generate intakes from the FFQ. Estimates were also within 2% of the National Nutrition Survey estimates for women in this age group (18).

Statistical analysis. We used *t* tests to compare group means for normally distributed variables and χ^2 tests to compare proportions. Multiple linear regression was used to investigate relations between maternal dietary composition during pregnancy and birth characteristics of the baby. We adjusted birth outcomes for gestational age of the baby because our interest was in small size for date, rather than prematurity. All statistical tests were two-tailed with an α of 0.05.

To determine whether macronutrient intakes influence birth size via a pathway other than energy production, energy intake must be taken into account. There is debate concerning how this should be done (19). Simply adjusting for total energy intake in a multivariate model, including grams of a particular macronutrient, is problematic because correlations between the 2 can inflate standard errors. Following the recommendations of Mackerras (19), we undertook our analyses using the nutrient density method in which energy from a macronutrient is expressed as a percentage of total energy intake. We also used the residual method described by Mackerras (19). Because the results were very similar, we report only those from the nutrient density method.

We planned to test specific hypotheses, rather than build a comprehensive model to predict birth size. Therefore, when deciding which variables to include in our regression analyses, we focused on those variables that could theoretically confound the hypothesized associations. To be a potential confounder, a variable had to be associated with maternal dietary quality and have an independent link with restricted fetal growth. Smoking clearly satisfies these criteria because it is associated with low birth weight, and smokers have been shown to have different diets from nonsmokers. Similarly, maternal age meets these criteria; however, sex of the baby does not.

It was not appropriate to treat socioeconomic status as a confounding variable because part of its influence may be due to poor maternal diet. To include socioeconomic status in a model would therefore be to overadjust. Instead, we identified specific variables, other than nutrition, through which socioeconomic disparities in birth outcomes might arise. Guided by the recent review of Kramer et al. (20), which distinguishes between factors influencing restricted fetal growth and those influencing premature birth, we considered other candidates for potential confounding to be the following: maternal height, prepregnancy weight, primiparity, alcohol consumption, and use of marijuana or cocaine. Although Kramer et al. (20) focused on alcohol consumption of >2 drinks/d, others found a reduction in birth weight if any alcohol was consumed (21). Because none of the women in our study reported consuming >2 drinks/d during pregnancy, we classified alcohol consumption as "any" or "none."

Although pregnancy-induced hypertension influences fetal growth, its link with maternal nutrition is tenuous. We therefore decided not to include it in the basic model, to conserve power, but to check for any confounding separately. Gestational diabetes was treated similarly. Conceptually, weight gain during pregnancy is problematic because it could be viewed as a mediating variable or as a confounder. We decided to undertake analyses with and without adjustment for this variable. In addition, we repeated all analyses excluding women with low prepregnancy weight (BMI < 20 kg/m²) to determine whether any effects were due primarily to this subgroup.

Regression analysis was undertaken for all participants with dietary data, then repeated for women who were considered to have "reliable" data. It was decided a priori that this meant that birth characteristics of the baby were complete and dietary data were realistic. These criteria are explained below.

We requested that midwifery staff at the 5 cooperating hospitals make special measurements of the baby and weigh the placenta, for all women participating in the study. In a proportion of cases, however, measurements for study purposes were overlooked. In these cases, we obtained the birth weight and length from routine hospital records, but because placental weights are not routinely recorded, birth details were incomplete in some cases.

Individuals vary in their ability to provide accurate dietary information. There are established equations for estimating the total energy an individual requires, based on weight, and also established additional requirements for pregnancy (22,23). Using this method, we calculated an energy requirement for each pregnant woman, based on her weight. When an individual's energy intake obtained from questionnaire data is greatly discrepant from the energy intake predicted by metabolic equations, it is customary to presume that the dietary questionnaire data do not reflect the actual food intake. We set a cutoff criterion for this difference at 70%, so that reported energy intake at least 1.7 times greater or 0.3 times less than the predicted energy requirement was considered implausible. This criterion was generous to allow for pregnancy influences, such as nausea or hunger, that affect women variously. Applying this condition, 37 individuals had unrealistic dietary data in early or late pregnancy.

RESULTS

A total of 605 women joined the study, representing 65% of women invited to participate. Of these, 557 women (92%) completed the study and gave birth between October 1998 and April 2000. The most common reason for women withdrawing from the study ($n = 48$) was miscarriage or termination of pregnancy ($n = 27$, 56% of withdrawals and 4% of the sample).

Table 1 describes the women who completed the study.

TABLE 1

*Characteristics of 556 pregnant women
in Adelaide, South Australia¹*

Characteristic	
Age, y	29 ± 5
Prepregnancy weight, kg	65.9 ± 15.0
BMI, kg/m ²	24.9 ± 5.7
Primiparous	187 (33.6)
Antenatal care in public hospital	301 (54.1)
Smoked prepregnancy	157 (28.2)
Smoked during pregnancy	109 (19.6)
Education	
Partial high school	189 (34.0)
Completed high school	82 (14.7)
Technical college qualification (but not necessarily completed high school)	168 (30.2)
University degree	101 (18.2)
Annual household income, \$AUD	
0-31,199	180 (32.4)
31,200-51,999	166 (29.9)
>52,000	200 (36.2)
Did not wish to answer	7 (1.3)
Employment	
Working full-time	134 (24.1)
Working part-time	162 (29.1)
Home duties	220 (39.6)
Unemployed	21 (3.8)
Other	19 (3.4)

¹ Values are means ± SD or n (%).

The dietary questionnaire from early pregnancy was lost in 1 case; thus this description of participants and the subsequent analyses concern 556 women. The ages of women involved in the study ranged from 18 to 41 y, with a mean of 29 y. Before pregnancy, 15% of women were underweight (BMI < 20 kg/m²), whereas 25% had a BMI of 30 kg/m² or more. The index pregnancy was the first (of at least 20 wk duration) for ~33% of the women and the second for a further 40%; ~90% of the women lived with their partner and just over half were receiving antenatal care through a public hospital. Participants' socioeconomic background is indicated by educational attainment, household income and, to a lesser extent, employment status, given that the majority of women already had at least 1 child to care for.

Women who declined participation ($n = 323$) had a mean age of 28 y (range 18 to 42 y) which was slightly lower than that of women who chose to be involved ($t = 2.1$, $P < 0.05$). Nonparticipants were similar to participants in terms of their parity. The mean area disadvantage score (24), based on postcode of residence, was ~0.75 SD lower for nonparticipants than participants (mean difference = 56, $t = 0.1$, $P < 0.05$).

Our sample is demographically similar to all women having children in South Australia. From routinely collected statewide data, 54% of women who gave birth in 1999 were aged <30 y and it was the first birth for 31% of women. Of these, 87% were married or in a de facto relationship and 45% received antenatal care at a hospital (13). From other government reports, ~50% of South Australian women with children < 4 y old are not employed (25), and among Australians aged 25-34 y in 1998, 34% had not completed high school, 15% completed high school but not further education, and 52% had some form of postschool qualification (26). In 1997-1998, the average weekly income of Australian couples with an eldest child < 5 y old was \$973, approximately \$50,600/y (27).

As described in Subjects and Methods, we planned to test our hypotheses using all participants and a subset who were considered to have "reliable" data, based on the plausibility of the dietary data and completeness of the birth data. Applying the prespecified criteria, 37 individuals had unrealistic dietary data in early or late pregnancy, and birth data were incomplete in 91 cases. Thus, data for 429 participants (77%) met the criteria for reliable data.

Dietary profiles of the women in our sample, in early and late pregnancy, are presented in Table 2. Of the early pregnancy assessments, 91% were made before 16 complete weeks of gestation, whereas 88% of late pregnancy dietary assessments were made between wk 30 and 34 of gestation. Four women delivered their babies prematurely and completed the "late pregnancy" interview shortly after the birth; 5 women did not complete the late pregnancy assessment of diet for similar reasons. Diets of women in the subgroup with reliable data are presented separately. As expected, given the criteria we used, in this subset, the daily total energy intake is reduced and interquartile ranges for other aspects of the diet are compressed.

Characteristics of the babies at birth are presented in Table 3. The distribution of birth weight is similar to that for all babies born in South Australia, with a mean birth weight of 3359 g in 1999 (13). Of babies in the study, 6% were born preterm, very similar to the proportion for South Australia as a whole (13). There are no notable differences between this description and that for babies born to women in the subset with reliable data.

Relations between maternal dietary composition in early pregnancy and birth characteristics of the baby (adjusted for

TABLE 2

Dietary composition of 556 women during pregnancy

Dietary component	Median	Lower quartile	Upper quartile
Early pregnancy			
Energy, MJ/d	9.0	7.2	11.6
Protein, g/d	89	67	112
Carbohydrate, g/d	273	213	349
Fat, g/d	79	60	106
% Energy from protein	16.6	14.8	18.1
% Energy from carbohydrate	48.3	44.5	53.5
% Energy from fat	33.1	28.5	36.6
Late pregnancy			
Energy, MJ	9.2	7.5	11.3
Protein, g	86	71	108
Carbohydrate, g	282	230	347
Fat, g	80	62	103
% Energy from protein	16.2	14.3	18.2
% Energy from carbohydrate	49.1	45.0	53.3
% Energy from fat	32.7	28.7	36.2
<i>Subgroup of 429 participants with reliable data</i>			
Early pregnancy			
Energy, MJ/d	8.8	7.2	11.0
Protein, g/d	87	68	107
Carbohydrate, g/d	265	211	338
Fat, g/d	77	60	99
% Energy from protein	16.6	14.8	18.1
% Energy from carbohydrate	48.1	44.4	53.5
% Energy from fat	33.0	28.3	36.6
Late pregnancy			
Energy, MJ	9.0	7.5	10.7
Protein, g	84	71	102
Carbohydrate, g	274	230	332
Fat, g	77	61	98
% Energy from protein	16.2	14.4	18.1
% Energy from carbohydrate	49.2	45.3	53.2
% Energy from fat	32.8	28.7	36.0

gestational age) were examined, taking into account potential confounding by maternal age, height, prepregnancy weight, primiparity, smoking, alcohol consumption, and recreational drug use (Table 4). Among all women with valid data, the proportion of maternal dietary energy derived from protein in early pregnancy was positively associated with birth weight and with placental weight (borderline statistical significance). Each isoenergetic 1% increase in protein consumption was associated with a 16-g increase in birth weight (95% CI, 2.8 to 29.2 g) and a 4.2 g increase in placental weight (95% CI, -0.4 to 8.5 g). No associations between the carbohydrate or fat content of the maternal diet in early pregnancy and birth size of the baby were evident among all participants.

However, when this analysis was restricted to the subgroup of participants considered to have reliable data (Table 4), the associations between the percentage of energy derived from protein and the outcomes of birth weight and placental weight were strengthened and a positive association between the contribution of protein to the maternal diet in early pregnancy and ponderal index of the baby was apparent ($P = 0.05$). In addition, a negative association between dietary carbohydrate content and ponderal index ($P = 0.04$) was observed.

In all, 37 women had gestational diabetes and 36 women had pregnancy hypertension. The associations did not change appreciably when women with these conditions were excluded or when adjustment was made; therefore, we did not adjust for

these conditions. Associations did not change when adjustment was made for weight gain during pregnancy. There was no evidence of differential effects depending on whether prepregnancy BMI was less or $>20 \text{ kg/m}^2$. We examined each analysis for a quadratic relation between maternal protein intake and birth size but did not find any evidence for detrimental effects of high protein intakes.

When protein intake in early pregnancy was divided into cereal, meat, and dairy sources (for which intercorrelations were low), no relations with birth characteristics were significant in the sample as a whole. However, among those participants considered to have reliable data, the percentage of energy from dairy protein was associated with birth weight and with ponderal index more strongly than protein from other sources, for which effects were not significant (both standardized regression coefficients = 0.11, $P < 0.05$). Each isoenergetic 1% increase in dairy protein consumption was associated with a 25-g increase in birth weight ($P = 0.02$) and a 0.12 kg/m^3 increase in ponderal index ($P = 0.05$). Associations between energy derived from the 3 forms of protein and placental weight were of similar magnitude and not significant when considered simultaneously.

Among all participants with valid data, no associations between maternal dietary components in late pregnancy and birth size were apparent (Table 4). However, among the subgroup of participants with reliable data, the percentage of energy derived from carbohydrate in late pregnancy was negatively associated with ponderal index. Each isoenergetic 1% increase in carbohydrate intake was associated with a decrease in ponderal index of 0.04 kg/m^3 (95% CI, -0.07 to 0).

DISCUSSION

Women in our study sample closely resembled the broader population of women having children in South Australia in terms of their family and socioeconomic circumstances and age. We excluded women with conditions that strongly affect fetal growth, such as multiple pregnancy or preexisting diabetes; currently women with these conditions account for $<5\%$ of those giving birth. Our dietary assessment method was appropriate only for Caucasian women, who account for $>90\%$ of births in the state; therefore, we did not include women of other ethnicity. Nevertheless, the birth characteristics of the babies in the study sample were very similar to those of babies born statewide.

Women were asked about their usual diet over the past 3 mo, on average at 14 wk of gestation. Each early pregnancy dietary profile thus reflects diet from around the time of conception. We found that dietary composition of women in early

TABLE 3

Characteristics at birth of 556 babies born to women in Adelaide, South Australia¹

Characteristic	Girls	Boys
<i>n</i>	283	273
Birth weight, g	3349 ± 574	3500 ± 472
Placental weight, ² g	573 ± 131	589 ± 136
Ponderal index, kg/m^3	27.2 ± 2.5	26.7 ± 2.6
Gestational age at birth, wk	39.4 ± 1.8	39.5 ± 1.5

¹ Values are means ± SD.

² Data for this variable were missing for 15% of girls and 17% of boys.

TABLE 4

Maternal dietary composition in pregnancy and birth dimensions of the baby

Dietary component	Birth weight		Placental weight		Ponderal index	
	b	P	b	P	b	P
Early pregnancy	n = 556		n = 446		n = 556	
% energy from protein	16.0	0.02*	4.1	0.07	0.05	0.16
% energy from carbohydrate	-2.1	0.4	-0.8	0.4	-0.02	0.18
% energy from fat	-0.3	0.9	-0.1	0.9	0.02	0.4
Late pregnancy	n = 551		n = 446		n = 551	
% energy from protein	3.4	0.6	1.4	0.5	0.02	0.6
% energy from carbohydrate	-1.3	0.6	-0.8	0.4	-0.02	0.2
% energy from fat	0.3	0.9	0.6	0.6	0.02	0.3
<i>Subgroup of 429 participants with reliable data</i>						
Early pregnancy						
% energy from protein	17.7	0.02*	4.9	0.04*	0.09	0.04*
% energy from carbohydrate	-2.4	0.4	-1.3	0.18	-0.03	0.07
% energy from fat	-0.6	0.9	0.3	0.8	0.02	0.2
Late pregnancy:						
% energy from protein	5.1	0.5	3.0	0.17	0.05	0.19
% energy from carbohydrate	-3.2	0.3	-1.5	0.12	-0.04	0.05*
% energy from fat	2.6	0.5	1.1	0.3	0.03	0.19

¹ Adjusted for maternal age, height, prepregnancy weight, primiparity, smoking, alcohol consumption, and recreational drug use; * $P \leq 0.05$.

pregnancy was associated with size of the baby at birth, independently of energy intake and weight gain. In particular, the percentage of energy derived from protein was positively related to birth weight and placental weight. These associations were not driven by effects among women whose prepregnancy weight was low. There was no evidence of a decline in birth weight above a certain protein level.

Maternal dietary composition in late pregnancy was largely unrelated to birth size of the baby, although there was an indication that high carbohydrate intake was linked to neonatal thinness. It is biologically plausible that nutritional effects on the fetus could vary with the time of pregnancy, because fetal development and nutrient needs are structured in time. Changes in nutritional needs have been identified even during the embryonic stage, with growth initially depending on simple molecules such as pyruvate, then being influenced more by amino acid concentrations (28). Glucose becomes a major fuel later in gestation (29). Animal experiments show that the consequences of nutritional interventions during pregnancy can depend on the timing (29). In women, for example, timing is clearly relevant in the requirement for folate periconceptually to prevent neural tube defects. Nutritional conditions may be especially important in early pregnancy, when placental function is established because inadequate maternoplacental supply often underlies later manifestation of growth failure (29).

We considered the influence of different energy sources, for a given energy intake, on birth size. In this context, an increase in energy derived from protein necessarily involves a decrease in that from carbohydrate or fat. We cannot say whether biological effects are attributable to more protein or less carbohydrate. However, our finding that sources of protein differ in effects is consistent with findings from several other studies of fetal growth. Godfrey and colleagues (9) reported that the positive association between maternal protein intake in late pregnancy and placental weight reflected dairy intake, whereas birth weight was more closely related to meat protein intake. Rao et al. (30), in a study of pregnant Indian women, observed that the frequency of consumption of milk and green

leafy vegetables was positively associated with birth dimensions of the baby. Chang et al. (31) found that dairy product intake among pregnant African-American adolescents had a positive effect on fetal femur growth and attributed this to the calcium content of dairy foods. Differences between protein sources in relation to placental or fetal growth could reflect differences in the micronutrient content, but could also be due to differences in amino acid composition and metabolic consequences. In studies of animals, for example, the type of protein fed to rats was shown to influence body weight, visceral fat storage, and insulin sensitivity (32).

Our results are based on dietary intakes assessed using an FFQ. We recognize that data obtained using this method are useful for ranking individuals but do not necessarily permit confident assessments of absolute intake. The 1995 National Nutrition Survey (18) showed that for Australian women aged 25–44 y, median daily energy intake was 7.6 kJ, and medians for protein, fat, and carbohydrate were 72, 66, and 210 g, respectively. The respective contributions of these macronutrients to dietary energy were 17, 33, and 47%. In our sample, dietary composition values were almost identical to the national figures, but the absolute intakes were higher. However, the absolute intakes were comparable to those of other groups of pregnant women (9,11).

When we restricted our analysis to individuals deemed to have the most reliable data, results were strengthened but did not change in nature, which is consistent with our understanding that there is a considerable degree of random error in FFQ data. Even within the subset of women with reliable data, the magnitude of effects may be underestimated. The FFQ method can be subject to systematic errors in reporting (bias), and although some researchers have found that this is less likely to affect results expressed as a percentage of energy intake [see, for example (33)], our results must be interpreted cautiously.

Since the 1930s, numerous surveys of maternal diet during pregnancy have been undertaken in Western settings, and many have extended longitudinally to investigate links with birth size. An absence of associations was often reported, but the sample size frequently appears inadequate. Among the

recent, sizeable studies are 2 conducted in the south of England, with dissimilar results. Godfrey et al. (9) assessed the diets of 538 pregnant women living in Southampton and reported negative associations between energy, carbohydrate, and fat consumption in early pregnancy and size of the baby and placenta at birth. No univariate associations with late pregnancy dietary intakes were observed, but after adjustment for early pregnancy carbohydrate intake, low protein intake in late pregnancy was associated with decreased placental and birth weights. Mathews et al. (11) studied 693 women in Portsmouth and found no significant effect of maternal nutrition on birth size. Some striking differences between these 2 studies were noted (34). One possibility is that the Portsmouth study had a greater degree of measurement error. The first dietary assessment was based on a 7-d diary, which is superior to an FFQ in validation studies involving conscientious individuals, but may not be in community-based samples (and 20% of the women recruited in Portsmouth did not complete it); the second assessment was based on an FFQ mailed to participants.

Subsequently, Sloan et al. (12) presented an analysis of data collected in the United States in 1983 as part of an evaluation of the Special Supplementation Program for Women, Infants and Children (the WIC program). Dietary intakes of >2000 women were estimated using the average values obtained in two 24-h dietary recalls obtained towards the middle and end of pregnancy. A quadratic relation between maternal protein intake and birth weight was observed, such that birth weight increased with protein intakes up to 70 g/d, but declined with higher protein intakes. However, in comparisons between groups, women who consumed "high" levels of protein (>85 g/d) were significantly lighter and had lower BMIs than women with "medium" and "low" intakes, both before and during pregnancy; their weight gain during pregnancy was similar, but they reported twice the energy intake of the low-protein group. The authors maintain that this discrepancy does not necessarily indicate the presence of reporting bias. In our study in which women were, on average, 1 kg heavier than those in the U.S. study, 48% consumed at least 85 g protein/d and ~70% consumed >70 g protein/d (bearing in mind the limitations of the FFQ in determining absolute intakes).

The possibility that maternal macronutrient balance can affect fetal growth and later health is supported by several long-term follow-up studies of children born to women whose diet during pregnancy was documented. Roseboom et al. (35) reported that among individuals who were in utero at the time of the Dutch famine in World War II, adult blood pressure was inversely related to the ratio of protein to carbohydrate in the mother's diet during the 3rd trimester of pregnancy. Campbell et al. (36) located some 200 men and women born in Aberdeen between 1948 and 1954, whose mothers had completed a dietary survey during pregnancy. When the mother's intake of animal protein during pregnancy had been <50 g/d, there was a positive association between maternal carbohydrate intake and blood pressure of the offspring at age 40 y; when maternal intake of protein was >50 g/d, the association was inverse. Shiell et al. (37) assessed the blood pressure of >500 individuals at age ~30 y born to women who had lived in Motherwell, UK, and been encouraged to consume a pound of meat per day during pregnancy; elevated blood pressure was observed among individuals whose mothers had high intakes of meat and fish but low carbohydrate during late pregnancy.

The Aberdeen and Motherwell studies suggest that a very high protein diet during pregnancy can have adverse effects. This is also the suggestion of the recently updated Cochrane systematic review of randomized controlled trials of various

forms of protein supplementation during pregnancy (38), although evidence from the 2 trials of high-protein supplementation (in which protein provided >25% of total energy) is insufficient for firm conclusions. The largest trial is the widely known work of Rush et al. (39), involving ~500 African-American women living in New York, all of whom were at risk of having a low-birth-weight baby (half because of low prepregnancy weight or low weight gain). The high-protein supplement was given after 30 wk of pregnancy. This does not correspond to the situation in our study in which results concerned usual diet in early pregnancy (and <1% of women in our sample derived >25% of their dietary energy from protein).

Moderate isoenergetic protein supplementation in which protein replaces an equal quantity of nonprotein energy was evaluated in 2 small trials concerning Asian women in Birmingham (40,41) and a trial involving >500 Chilean women (42). Collectively, these 3 trials do not provide evidence that isoenergetic protein supplementation is beneficial for birth weight (38). (In fact, the Chilean study indicated that supplementation increased the risk of a baby being born small for gestational age, but methodological problems make this result unreliable.) Changing a woman's nutritional plane during pregnancy may be detrimental to the fetus (43), and our results do not necessarily lend support to some form of supplementation in pregnancy.

In summary, we showed that, in a Western setting, the composition of a woman's diet during pregnancy is related to the size of the baby and placenta at birth. This pattern was observed in women regardless of their weight before pregnancy, the amount eaten, and the weight gained during pregnancy. Consistent with findings from animal models, the balance between protein and carbohydrate was important; this may signify benefits of protein or of accompanying micronutrients. Given the disappointing results of supplementation during pregnancy, the extent to which these findings reflect effects of diet before pregnancy deserves investigation.

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LITERATURE CITED

1. Kramer, M. S. (1998) Maternal nutrition, pregnancy outcome and public health policy. *Can. Med. Assoc. J.* 159: 663-665.
2. Kramer, M. S. (2003) The epidemiology of adverse pregnancy outcomes: an overview. *J. Nutr.* 133: S1592-S1596.
3. Kramer, M. S. (1998) Socioeconomic determinants of intrauterine growth retardation. *Eur. J. Clin. Nutr.* 52: S29-S32.
4. Rosso, P. (1990) *Nutrition and Metabolism in Pregnancy*. Oxford University Press, New York, NY.
5. Susser, M. (1991) Maternal weight gain, infant birth weight, and diet: causal sequences. *Am. J. Clin. Nutr.* 53: 1384-1396.
6. Barker, D.J.P., ed. (1992) *Fetal and Infant Origins of Adult Disease*. British Medical Journal Books, London, UK.
7. Hoet, J. J. & Hanson, M. A. (1999) Intrauterine nutrition: its importance during critical periods for cardiovascular and endocrine development. *J. Physiol.* 514: 617-627.

8. Barker, D.J.P. (2003) The developmental origins of adult disease. *Eur. J. Epidemiol.* 18: 733–736.
9. Godfrey, K., Robinson, S., Barker, D.J.P., Osmond, C. & Cox, V. (1996) Maternal nutrition in early and late pregnancy in relation to placental and fetal growth. *Br. J. Obstet. Gynaecol.* 104: 410–414.
10. Godfrey, K. M., Barker, D.J.P., Robinson, S. & Osmond, C. (1997) Maternal birthweight and diet in pregnancy in relation to the infant's thinness at birth. *Br. J. Obstet. Gynaecol.* 104: 663–667.
11. Mathews, F., Yudkin, P. & Neil, A. (1999) Influence of maternal nutrition on outcome of pregnancy: prospective cohort study. *Br. Med. J.* 319: 339–343.
12. Sloan, N. L., Lederman, S. A., Leighton, J., Himes, J. H. & Rush, D. (2001) The effects of prenatal dietary protein intake on birth weight. *Nutr. Res.* 21: 129–139.
13. Chan, A., Scott, J., Nguyen, A.-M. & Keane, R. (2000) Pregnancy Outcome in South Australia 1999. Pregnancy Outcome Unit, Epidemiology Branch, Department of Human Services, Adelaide, SA.
14. Bingham, S. A. (1997) Dietary assessment in the European prospective investigation of diet and cancer (EPIC). *Eur. J. Cancer Prev.* 1: 118–124.
15. Lewis, J. & Holt, R. (1992) NUTTAB91–92: Commonwealth Government of Australia. National Food Authority, Canberra, ACT.
16. Nelson, M., Black, A. E., Morris, J. A. & Cole, T. J. (1989) Between- and within-subject variation in nutrient intake from infancy to old age: estimating the number of days required to rank dietary intakes with desired precision. *Am. J. Clin. Nutr.* 50: 155–167.
17. Masson, L. F., McNeill, G., Tomany, J. O., Simpson, J. A., Peace, H. S., Wei, L., Grubb, D. A. & Bolton-Smith, C. (2003) Statistical approaches for assessing the relative validity of a food-frequency questionnaire: use of correlation coefficients and the kappa statistic. *Public Health Nutr.* 6: 313–321.
18. McLennan, W. & Podger, A. (1998) National Nutrition Survey, Nutrient Intakes and Physical Measurements, Australia 1995. ABS Catalogue Number 4805.0. Australian Bureau of Statistics, Canberra, ACT.
19. Mackerras, D. (1996) Energy adjustment: the concepts underlying the debate. *J. Clin. Epidemiol.* 49: 957–962.
20. Kramer, M. S., Seguin, L., Lydon, J. & Goulet, L. (2000) Socio-economic disparities in pregnancy outcome: why do the poor fare so poorly? *Pediatr. Perinat. Epidemiol.* 14: 194–210.
21. Holman, C. D., English, D. R., Bower, C. & Kurinczuk, J. J. (1996) NHMRC recommendations on abstinence from alcohol in pregnancy. National Health and Medical Research Council. *Med. J. Aust.* 164: 699.
22. Schofield, W. N. (1985) Predicting basal metabolic rate, new standards and review of previous work. *Hum. Nutr. Clin. Nutr.* 39: S5–S41.
23. Shetty, P. S., Henry, C. J., Black, A. E. & Prentice, A. M. (1996) Energy requirements of adults: an update on basal metabolic rates (BMRs) and physical activity levels (PALs). *Eur. J. Clin. Nutr.* 50: S11–S23.
24. McLennan, L. (1990) Socio-Economic Indexes for Areas. ABS Catalogue Number 1356.0. Australian Government Publishing Service, Canberra, ACT.
25. Australian Bureau of Statistics (2000) Australian Social Trends. ABS Catalogue Number 4102.0. Australian Government Publishing Service, Canberra, ACT.
26. Australian Bureau of Statistics (2000) Transition from Education to Work. ABS Catalogue Number 6227.0. Australian Government Publishing Service, Canberra, ACT.
27. Australian Bureau of Statistics (1999) Income Distribution, Australia. ABS Catalogue Number 6523.0. Australian Government Publishing Service, Canberra, ACT.
28. Martin, P. M., Sutherland, A. E., Van Winkle, L. J. (2003) Amino acid transport regulates blastocyst implantation. *Biol. Reprod.* 69: 1101–1108.
29. Harding, J. E. (2001) The nutritional basis of the fetal origins of adult disease. *Int. J. Epidemiol.* 30: 15–23.
30. Rao, S., Yajnik, C. S., Kanade, A., Fall, C.H.D., Margetts, B. M., Jackson, A. A., Shier, R., Joshi, S., Rege, S. et al. (2001) Intake of micronutrient-rich foods in rural Indian mothers is associated with the size of their babies at birth: Pune Maternal Nutrition Study. *J. Nutr.* 131: 1217–1224.
31. Chang, S.-C., O'Brien, K. O., Nathanson, M. S., Caulfield, L. E., Mancini, J. & Witter, F. R. (2003) Fetal femur length is influenced by maternal dairy intake in pregnant African American adolescents. *Am. J. Clin. Nutr.* 77: 1248–1254.
32. Belobrajdic, D., McIntosh, G. & Owens, J. (2003) The effects of dietary protein on rat growth, body composition and insulin sensitivity. *Asia Pac. J. Clin. Nutr.* 12: S42.
33. Smith, W. T., Webb, K. L. & Heywood, P. F. (1994) The implications of underreporting in dietary studies. *Aust. J. Public Health* 18: 311–314.
34. Symonds, M. E., Budge, H. & Stephenson, T. (2000) Limitations of models used to examine the influence of nutrition during pregnancy and adult disease. *Arch. Dis. Child.* 83: 215–219.
35. Roseboom, R. J., van der Meulen, J.H.P., van Montfrans, G. A., Ravelli, A.C.J., Osmond, C., Barker, D.J.P. & Bleker, O. P. (2001) Maternal nutrition during gestation and blood pressure in later life. *J. Hypertens.* 19: 29–34.
36. Campbell, D. M., Hall, M. H., Barker, D.J.P., Cross, J., Shiell, A. W. & Godfrey, K. M. (1996) Diet in pregnancy and the offspring's blood pressure 40 years later. *Br. J. Obstet. Gynaecol.* 103: 273–280.
37. Shiell, A. W., Campbell-Brown, M., Haselden, S., Robinson, S., Godfrey, K. M. & Barker, D.J.P. (2001) A high meat, low carbohydrate diet in pregnancy: relation to adult blood pressure in the offspring. *Hypertension* 38: 1282–1288.
38. Kramer, M. S. & Kakuma, R. (2004) Energy and protein intake in pregnancy (Cochrane Review). In: *The Cochrane Library*, Issue 1. John Wiley & Sons, Chichester, U.K.
39. Rush, D., Stein, Z. & Susser, M. (1980) A randomized controlled trial of prenatal nutrition supplementation in New York City. *Pediatrics* 65: 683–697.
40. Viegas, O.A.C., Scott, P. H., Cole, T. J., Mansfield, H. N., Wharton, P. & Wharton, B. A. (1982) Dietary protein energy supplementation of pregnant Asian mothers at Sorrento, Birmingham. I. Unselective during second and third trimesters. *Br. Med. J.* 285: 589–592.
41. Viegas, O.A.C., Scott, P. H., Cole, T. J., Eaton, P., Needham, P. G. & Wharton, B. A. (1982) Dietary protein energy supplementation of pregnant Asian mothers at Sorrento, Birmingham. II. Selective during third trimester only. *Br. Med. J.* 285: 592–595.
42. Mardones-Santander, F., Rosso, P., Stekel, A., Ahumada, E., Llaguno, S. & Pizzaro, F. (1988) Effect of a milk-based food supplement on maternal nutritional status and fetal growth in underweight Chilean women. *Am. J. Clin. Nutr.* 47: 413–419.
43. Harding, J. E., Owens, J. A. & Robinson, J. S. (1992) Should we try to supplement the growth retarded fetus? A cautionary tale. *Br. J. Obstet. Gynaecol.* 99: 707–710.