

Physiology of pregnancy and nutrient metabolism¹⁻³

Janet C King

ABSTRACT Pregnancy consists of a series of small, continuous physiologic adjustments that affect the metabolism of all nutrients. The adjustments undoubtedly vary widely from woman to woman depending on her prepregnancy nutrition, genetic determinants of fetal size, and maternal lifestyle behavior. Studies of protein and energy metabolism illustrate the potential of adjusting the use of those nutrients to conserve a fetal supply. Adjustments in the metabolism of nitrogenous compounds are in place by the second quarter of pregnancy. During the last quarter of pregnancy, when fetal demands are greatest, those adjustments allow a positive nitrogen retention. The energy requirement of basal metabolism is influenced by maternal prepregnant nutrition and by fetal size. If maternal energy reserves are low at conception, the basal metabolic rate is down-regulated to conserve energy. Also, women having larger babies tend to have greater increases in their basal metabolic rate and lower rates of maternal energy storage. Changes in maternal food and physical activity behaviors during gestation may augment the physiologic adjustments. However, the substantial variability in food intakes and physical activity makes it difficult to show those changes. Thresholds in the capacity to adjust nutrient use to the amount supplied exist for all nutrients. When intakes fall below the threshold, fetal growth and development is affected more than is maternal health. Efforts to achieve good maternal nutritional status preconception as well as throughout gestation best assure a good milieu for fetal growth and development. *Am J Clin Nutr* 2000;71(suppl):1218S-25S.

KEY WORDS Pregnancy, protein, energy, basal metabolism, food intake, physical activity, physiology

INTRODUCTION

Pregnancy is a dynamic, anabolic state. Within several weeks of conception, a new endocrine organ, the placenta, is already formed and is secreting hormones that affect the metabolism of all nutrients. These adjustments in nutrient metabolism, in addition to changes in the anatomy and physiology of the mother, support fetal growth and development while maintaining maternal homeostasis and preparing for lactation. Depending on the nutrient, one or more of the following adjustments occur: 1) accretion in new tissue or deposition in maternal stores, 2) redistribution among tissues, and 3) increased turnover or rate of metabolism.

To support these adjustments, the use of nutrients from the diet may be altered either by increasing intestinal absorption or by reducing excretion via the kidney or gastrointestinal tract.

These adjustments in nutrient metabolism are complex and evolve continuously throughout pregnancy. The changes in nutrient metabolism can be described by several general concepts: adjustments in nutrient metabolism are driven by hormonal changes, fetal demands, and maternal nutrient supply; more than one potential adjustment exists for each nutrient; maternal behavioral changes augment physiologic adjustments; and a limit exists in the physiologic capacity to adjust nutrient metabolism to meet pregnancy needs, which when exceeded, fetal growth and development are impaired. The purpose of this review was to discuss these statements and to provide examples of the general changes that occur in nutrient metabolism during pregnancy.

HORMONAL CHANGES, FETAL DEMAND, AND MATERNAL NUTRIENT SUPPLY INFLUENCE NUTRIENT ADJUSTMENTS

Although pregnancy is a continuum of small physiologic adjustments, the changes are often grouped by period of gestation, ie, the first and last halves, the 3 trimesters, or the 4 quarters of pregnancy. Hytten and Chamberlain (1) provide an excellent summary of the physiologic adjustments in pregnancy in their book, *Clinical Physiology in Obstetrics*.

The first half of pregnancy is primarily a time of preparation for the demands of rapid fetal growth that occur later in pregnancy. The corpus luteum and the placenta secrete hormones that maintain pregnancy and influence metabolism. Human chorionic gonadotropin is detected in the serum and urine within a few days of implantation (**Table 1**) (2). Serum concentrations increase rapidly during early pregnancy to a peak occurring ≈ 60 d postconception. Thereafter, serum concentrations decrease as quickly as they increased until a relatively low serum concentration is reached and maintained to term. Human chorionic gonadotropin maintains the corpus luteum in early pregnancy; it has few known effects on nonreproductive tissues.

Human placental lactogen increases progressively throughout pregnancy. The precise function of human placental lactogen is not clear; however, because it is biologically similar to growth hormone, it may represent some type of growth factor for the

¹From the Western Human Nutrition Research Center, University of California, Davis.

²Presented at the symposium Maternal Nutrition: New Developments and Implications, held in Paris, June 11-12, 1998.

³Address reprint requests to JC King, Western Human Nutrition Research Center, University of California, Davis, CA 95616. E-mail: jking@whnrc.usda.gov.

fetus and the placenta (2). Serum concentrations correlate with placental mass. Human placental lactogen also affects carbohydrate and lipid metabolism.

Biosynthesis of the estrogens (ie, estrone, estradiol, and estriol) is a complicated process involving the mother, fetus, and placenta. In addition to influencing the uterus and other reproductive organs, estrogens cause a rise in certain binding hormones, which result in the elevation of total hormone concentrations, whereas the amounts of unbound and biologically active hormones remain unchanged. Estrogens also influence carbohydrate, lipid, and bone metabolism. Progesterone concentrations rise progressively throughout pregnancy, of which the initial source is the corpus luteum, but placental sources of progesterone predominate later during pregnancy. Progesterone relaxes smooth muscle, which causes atony of the gastrointestinal and urinary tracts.

Although fetal demand for nutrients occurs primarily during the last half of gestation when >90% of the fetal growth occurs, adjustments in nutrient metabolism are apparent within the first weeks of pregnancy (1). After the first 10 wk of pregnancy, serum triacylglycerol concentrations in pregnant women are 20% higher than those of nonpregnant women; they reach a value ≈ 3 times that of nonpregnant women by term. Other serum lipids (ie, phospholipids, cholesterol, glycerol, and fatty acids) also increase during pregnancy, but the net change is less than that of triacylglycerol. Circulating concentrations of most nutrients decrease by the end of the first 10 wk of gestation and remain lower than nonpregnant values until term. This decrease in circulating nutrients occurs before there is an increase in plasma volume. Serum albumin decreases ≈ 8 –10% in the first 10 wk of pregnancy. Because albumin is a carrier protein for many nutrients, the marked decline in albumin early in pregnancy may explain the sudden decrease in circulating nutrient concentrations. The net increase in plasma volume rises from 50 mL at 10 wk gestation to 800 mL at 20 wk gestation. Although the concentration of nutrients in the circulation declines during the same period of time, the reduction is less than the 40-fold change in plasma volume. Thus, the total amount of vitamins and minerals in circulation increases during pregnancy.

The rapid rate of fetal growth during the last half of gestation dictates changes in basal metabolism, protein, and mineral accretions. About 60% of the increase in basal metabolic rate (BMR) occurs during the last half of gestation, when the metabolic cost of fetal tissue synthesis is the greatest. Maternal fat stores are gained primarily between the 10th and 30th wk of gestation before fetal energy demands are at their peak. Approximately 3.3 kg fat is deposited in maternal stores, providing an energy reserve of ≈ 30000 kcal (129 MJ); the remaining 0.5 g fat is deposited in the fetus.

Protein metabolism in early and late pregnancy

Shifts in protein metabolism are complex and change gradually throughout gestation so that nitrogen conservation for fetal growth achieves full potential during the last quarter of pregnancy. Denne et al (3) showed the complexity of metabolic adjustments in nitrogenous compounds with the use of nitrogen and carbon stable isotopes. These detailed studies help explain the results of many nitrogen balance studies that have been conducted with pregnant women. Calloway (4) summarized the results of 17 nitrogen balance studies representing over 200 measurements, calculating a nitrogen retention of ≈ 1.3 g/d

between 20 and 40 wk of gestation, which is slightly more than the predicted nitrogen retention of 1.0 g/d (1).

A greater rate of nitrogen retention than the predicted need led investigators to propose that the mother gains additional protein in her own tissues. Naismith (5) first studied this issue in pregnant rats. He found that dams gained enough protein during the first 2 wk of pregnancy to increase maternal lean body mass by 8%. Maternal tissue catabolism then ensued during the third week of gestation, causing a loss of the lean tissue gained earlier in pregnancy.

To determine whether women gain lean tissue during early pregnancy as do rodents, Marino (6) studied nitrogen metabolism in 3 groups of women: 6 women were between 10 and 20 wk of gestation (the early pregnancy group; EP), 4 women were between 30 and 40 wk of gestation (the late pregnancy group; LP), and 6 women were nonpregnant (NP). All subjects were healthy, nonsmoking, nonvegetarian women between the ages of 20 and 35 y, and none abused drugs or alcohol. The women were confined to a metabolic unit for the 21-d study. All women were fed a diet that met the 1980 recommended dietary allowances for pregnancy (7). The NP group were fed the same diet as the pregnant women. The diet consisted of a semipurified liquid formula and a few whole food items, eg, beef broth and zwieback crackers. A trace mineral solution and vitamin and mineral capsules were given to supply recommended intakes of micronutrients. All urinary and fecal output was collected and analyzed for nitrogen content by use of the micro-Kjeldahl method (8). To estimate the loss of nitrogen through the integument, subjects wore a cotton suit for 3 d, and nitrogen losses in sweat and sloughed skin cells were estimated from the nitrogen content of the laundry and bath water of the subject. A one-way ANOVA was used to determine whether measures of nitrogen metabolism differed among the 3 groups of subjects.

The LP women retained ≈ 4 times as much nitrogen as the EP and NP subjects; the nitrogen retention of the EP and NP women averaged ≈ 0.5 g N/d. There was no evidence that women deposit nitrogen in early gestation to be mobilized later. The increased nitrogen retention in late pregnancy was due to a reduction in urinary nitrogen excretion (Table 2). The urinary nitrogen excretion of the LP women averaged 1.5 g less than that of the NP and EP women. There were no significant differences in fecal or integumental nitrogen losses in the 3 groups.

The reduction in urinary nitrogen excretion in late pregnancy was due to a decrease in urea excretion. Urea nitrogen accounted for 77% of the total urinary nitrogen output in the LP women and accounted for 83% and 87% of the total urinary nitrogen output in EP and NP women, respectively. All values differed significantly from each other (Table 3). Although nitrogen retention did not increase in EP women, their urea nitrogen excretion was significantly lower than that of NP women. This reduction in urinary urea nitrogen was offset by an increase in the excretion of uric acid, ammonia, and creatinine so that total nitrogen losses in EP and NP women were similar.

A decrease in urea synthesis seems to account for the reduction in urinary urea nitrogen in late pregnancy. Using ^{15}N as a tracer, Kalhan (9) found that the rate of urea synthesis declines by 30% in women during the first trimester of pregnancy compared with that of nonpregnant control subjects, and declines by 45% in women by the third trimester of pregnancy. Additionally, a greater decline in the plasma concentrations of urea cycle amino acids (eg,



TABLE 1Adjustments in circulating hormones, nutrient metabolism, and maternal tissue gain during pregnancy¹

	Time of Gestation			
	10 wk	20 wk	30 wk	40 wk
Serum placental hormones				
Human chorionic gonadotropin ($\times 10^4$ U/L)	1.3	4.0	3.0	2.5
Human placental lactogen (nmol/L)	23.148	138.888	254.628	393.516
Estradiol (pmol/L)	5.507	22.026	55.065	66.078
Progesterone (nmol/L)	79.5	159.0	318.0	413.4
Nutrient metabolism				
Basal metabolism, net change (MJ/d)	0.19	0.41	0.62	0.95
Serum albumin (g/L)	32	29	28	28
Serum triacylglycerol (%) ²	120	150	210	280
Serum alpha tocopherol (%) ²	110	120	135	150
Serum vitamin A (%) ²	75	75	75	75
Serum vitamin C (%) ²	85	75	68	62
Serum folic acid (%) ²	78	68	60	58
Products of conception				
Fetus (g)	5	300	1500	3400
Placenta (g)	20	170	430	650
Amniotic fluid (g)	30	250	750	800
Maternal tissue gain				
Uterus (g)	140	320	600	970
Mammary gland (g)	45	180	360	405
Plasma Volume (mL) ³	50	800	1200	1500
Total nutrient accretion in mother and fetus				
Protein (g)	36	165	498	925
Fat (g)	328	2064	3594	3825
Calcium (g)	—	—	—	30
Iron (mg)	—	—	—	565
Zinc (mg)	—	—	—	100

¹Data from reference 1.²Percentage of prepregnancy value.³For multigravidae.

citrulline, ornithine, and arginine) in EP and LP women than in NP women in the fasting state or after a standardized test meal supports a reduction in urea synthesis (Table 4). Alanine concentrations, a primary source of amino nitrogen for hepatic urea synthesis, were lower in EP and LP women than in NP women.

The excretion of the other nitrogenous compounds (eg, ammonia, creatinine, and uric acid) also increased during pregnancy (Table 3). Excretion was higher in EP than in NP women and was higher in LP than in EP women. A rise in the glomerular filtration rate is thought to account for the increased excretion of these compounds. At 16 wk gestation, insulin clearance is increased by $\approx 50\%$; it is $\approx 80\%$ higher than nonpregnant values by term (1). Because the glomerular filtration rate increases without substantial alterations in the production of creatinine and urea, plasma concentrations of these solutes decrease.

These alterations in protein metabolism during late pregnancy favor nitrogen conservation. The decline in total nitrogen excretion during late pregnancy suggests that amino acids are conserved for tissue synthesis. The sum total of plasma amino acids declines $\approx 15\text{--}25\%$, reflecting enhanced placental uptake (Table 4). Additionally, maternal oxidation of branched-chain amino acids for energy decreases in late gestation, increasing the amount of energy available for transfer to the fetus (10).

Because there is no evidence that pregnant women store protein early in gestation for later fetal demands, the increased requirements of late pregnancy must be met by physiologic

adjustments that enhance dietary protein utilization. If the dietary supply is low, a greater change in the physiologic adjustments is necessary to meet fetal needs than if dietary intake is liberal. The effect of low intakes of dietary protein on urea synthesis or on circulating concentrations of amino acids has not been studied in pregnant women. Studies of the response of the BMR to various energy intakes show that the maternal nutrient supply influences the physiologic response to pregnancy (11). For example, women with low energy intakes fail to increase their BMR until the last quarter of pregnancy. However, if the dietary supply is liberal, the BMR increases by

TABLE 2Nitrogen intake, losses, and retention in early pregnant (10–20 wk), late pregnant (30–40 wk), and nonpregnant women¹

Nitrogen source	Early pregnant	Late pregnant	Nonpregnant
	<i>n</i> = 6	<i>n</i> = 4	<i>n</i> = 6
	<i>g/d</i>		
Intake	12.03 \pm 0.24	12.19 \pm 0.04	11.88 \pm 0.46
Fecal	0.82 \pm 0.25	0.92 \pm 0.09	0.64 \pm 0.09
Urinary	10.52 \pm 1.15 ^a	9.02 \pm 0.97 ^b	10.56 \pm 0.09 ^a
Integumental	0.14 \pm 0.04	0.18 \pm 0.06	0.21 \pm 0.12
Retention	0.56 \pm 0.88 ^a	2.10 \pm 0.74 ^b	0.46 \pm 0.28 ^a

¹ $\bar{x} \pm$ SD. Data from reference 6. Values with different superscript letters are significantly different, $P < 0.05$.

TABLE 3

Excretion of total urinary nitrogen and urinary nitrogenous compounds in early pregnant (10–20 wk), late pregnant (30–40 wk), and nonpregnant women¹

Nitrogen	Early pregnant	Late pregnant	Nonpregnant
	<i>n</i> = 6	<i>n</i> = 4	<i>n</i> = 6
Total urinary (g/d)	10.52 ± 1.15 ^{a,b}	9.02 ± 0.97 ^a	10.56 ± 0.42 ^b
Urea (% of total)	83 ± 3.7 ^a	77 ± 1.3 ^b	87 ± 1.8 ^c
Ammonia (% of total)	6.8 ± 1.3 ^{a,b}	8.0 ± 0.2 ^a	5.7 ± 0.3 ^b
Creatinine (% of total)	4.3 ± 0.7 ^{a,b}	5.0 ± 0.5 ^a	3.8 ± 0.5 ^b
Uric acid (% of total)	1.6 ± 0.4 ^a	2.3 ± 0.2 ^b	1.1 ± 0.1 ^c

¹ $\bar{x} \pm$ SD. Data from reference 6. Values with different superscript letters are significantly different, $P < 0.05$.

the end of the first trimester. Presumably, maternal protein status at conception also influences the physiologic adjustments made in nitrogen metabolism. Future studies of nutrient metabolic adjustments in women consuming marginal to adequate diets are needed to fully understand the interactions among the physiology of pregnancy, nutrient metabolism, and maternal nutritional status.

MORE THAN ONE METABOLIC ADJUSTMENT IS AVAILABLE FOR EACH NUTRIENT

Fetal demands may double nutrient requirements. To protect fetal development, several mechanisms have evolved to ensure that fetal nutrient needs are met. For example, the cumulative energy needed for the increase in basal metabolism throughout gestation is ≈ 151 MJ (36 000 kcal); the daily energy need during the last quarter of pregnancy is ≈ 0.97 MJ (230 kcal) (1). To conserve energy to meet this demand, one or more of the following changes may occur: 1) reduction in the rate of lipid synthesis and maternal fat storage, 2) alteration in the intensity of physical activity, and 3) increases in food consumption and, therefore, increases in energy intakes.

Because energy metabolism may be adjusted in more than one way, the response of women who seem to enter pregnancy in similar nutritional states varies widely. This is apparent from the data of 10 women carefully evaluated at 5 different time points during their reproductive cycles: preconception; 8–10, 24–26, and 34–36 wk gestation; and 4–6 wk postpartum (12). All women were between 90% and 120% of their standard body weight preconception, had an average age of 29 y, and were having either their second or third child. At each time point, energy intake was estimated from a 3-d weighed food intake

record; resting metabolic rate was measured by indirect calorimetry in the morning before any food was eaten. The gain in body fat was estimated from measures of body density and total body water. Cumulative energy expenditure for resting metabolic rate, gain in fat mass, and gain in fat-free mass ranged from 252 to 714 MJ (60 000–170 000 kcal) (**Figure 1**). The theoretical energy need is thought to be ≈ 336 MJ (800 000 kcal) and only 2 of the 10 women expended close to that amount. The amount of energy expended for these 3 functions (ie, resting metabolic rate, fat gain, and fat-free mass gain) varied widely in the women. The net cost for resting metabolism ranged from no increase to a total of ≈ 462 MJ (110 000 kcal). The need for fat gain ranged from 0 to 504 MJ (120 000 kcal). If the energy cost was distributed over the entire 280 d of pregnancy, the additional energy need for these 10 healthy, normal-weight women would range from 0.88 to 2.39 MJ (210 to 570 kcal/d). Most of the women expended more than the additional 1.26 MJ (300 kcal) recommended for pregnant women.

Several relations are evident from this study. Higher cumulative increases in resting metabolism were associated with larger birth weights and a tendency for lower amounts of fat gain (**Figure 2**). Subject 7, who had the largest net increase in resting metabolic rate, did not gain any fat and delivered the largest baby (4.5 kg). She also reduced her physical activity by ≈ 2.3 MJ/d (550 kcal/d) during gestation. The subject with the smallest increase in resting metabolic rate (subject 3) delivered an infant weighing 3.07 kg and actually increased her physical activity by ≈ 2.9 MJ/d (700 kcal/d). The marked differences in metabolic responses of these women, who seemed to be of similar metabolic standing at conception, suggest that fetal size and, therefore, energy demand, influences the adjustments in energy metabolism made by the mother during gestation.

Energy metabolism and fetal growth also depends on the prepregnancy energy status of the mother and the quality of her living conditions during pregnancy (11). Underweight women living under the constraints of a limited food supply and under the demands of hard physical work, such as women in the Gambia, are unable to increase their food intake during gestation, and must maintain a high level of physical activity for survival. Such women frequently enter pregnancy with little to no maternal fat reserves (13). Their only option is to reduce their BMR to conserve energy for their fetus. This permits delivery of a viable infant who may or may not be growth retarded, depending on the severity of the situation.

Overweight women living in developed countries with sedentary lifestyles and with free access to a plentiful food supply represent the other extreme of living conditions. Longitudinal

TABLE 4

Plasma alanine and urea cycle amino acid concentrations in early pregnant (10–20 wk), late pregnant (30–40 wk), and nonpregnant women¹

Amino acid	Early pregnant		Late pregnant		Nonpregnant	
	Fasting	60 min postprandial	Fasting	60 min postprandial	Fasting	60 min postprandial
	$\mu\text{mol/L}$					
Alanine	321 ± 58 ^a	376 ± 100 ^a	321 ± 47 ^a	392 ± 68 ^a	407 ± 66 ^b	517 ± 29 ^b
Citrulline	24 ± 6 ^a	24 ± 3 ^a	29 ± 9 ^a	29 ± 8 ^a	43 ± 11 ^b	33 ± 6 ^b
Ornithine	23 ± 5 ^a	24 ± 6 ^a	21 ± 4 ^a	23 ± 4 ^a	50 ± 4 ^b	51 ± 6 ^b
Arginine	51 ± 10 ^a	53 ± 14 ^a	39 ± 8 ^a	50 ± 15 ^a	79 ± 10 ^b	97 ± 14 ^b
Total	2534 ± 334 ^a	2490 ± 400 ^a	2294 ± 256 ^a	2520 ± 396 ^a	3009 ± 312 ^b	3252 ± 251 ^b

¹ $\bar{x} \pm$ SD. Data from reference 6. Values with different superscript letters are significantly different, $P < 0.05$.



studies of these women have not been conducted, but a small cross-sectional study showed that the mass-specific rates of basal metabolism were $\approx 20\%$ higher in overweight pregnant women than in overweight nonpregnant women (14). Because these women enter pregnancy with ample fat stores, basal metabolism may increase to offset the accumulation of further fat stores.

This variability in energy expenditure during pregnancy makes it difficult to set standards for energy intake. For normal-weight and overweight women living in developed countries, the additional energy need may be < 1.26 MJ (300 kcal/d), especially if activity levels decline. An increase in food intake above that needed for the rise in basal metabolism that occurs during pregnancy will likely cause an excessive gain of body fat. In underweight women with limited access to food supplies and who are under the demands of physical labor, the consumption of food supplements, even for as short a duration as the last 90 d of pregnancy, may benefit fetal growth (15). The better the energy supply in this situation, the better the support for fetal growth and metabolic demands. Genetic factors determine the limits of fetal needs. Energy in excess of fetal needs has a high potential to be stored as maternal fat because of the overall anabolic milieu of pregnancy.

A variety of mechanisms for meeting the additional needs of other nutrients also exist. For example, the calcium demand of ≈ 300 mg/d during the last quarter of pregnancy may be met by a marked increase in the efficiency of calcium absorption and by the rates of bone resorption. In women with ample dietary supplies of calcium, urinary calcium excretion increases during gestation and contributes to the total calcium need for pregnancy. However, the net increase of urinary calcium excretion is quite variable. In a longitudinal study of 14 women followed from pre-conception to the third trimester of pregnancy, the net change in urinary calcium varied 6-fold, from ≈ 50 to > 300 mg/d (16). In addition to fetal demand and adjustments in calcium absorption and bone calcium release, several other factors contribute to this variation, ie, changes in dietary calcium intake, increases in plasma volume and glomerular filtration, and hormonal response.

The potential for diverse responses in nutrient metabolism complicates the assessment of the nutritional status of pregnant women. Pregnancy-specific standards for nutritional status need to be developed for each nutrient. However, it is also important that the standards should be established in women who enter pregnancy with good nutritional reserves, who have free access to an adequate food supply during pregnancy, and who deliver infants weighing between 3 and 4 kg. Efforts to date to define biochemical indicators of nutritional status during pregnancy failed to consider prepregnant nutritional status and birth weight. Future guidelines for nutrition during pregnancy should come from populations of healthy women who enter pregnancy in good nutritional status and who have had good pregnancy outcomes.

MATERNAL BEHAVIORAL CHANGES AUGMENT PHYSIOLOGIC ADJUSTMENTS

Changes in food intake and in physical activity behavior during pregnancy may affect the amount of energy and nutrients available for fetal growth. Behavior may be affected in 2 ways: there may be a change in the amount of food consumed or energy expended, or there may be a change in food choices or type of physical activity.

Changes in the amount of energy and nutrients consumed are difficult to detect because such changes tend to be relatively small

and dietary assessment methods are rather imprecise. Longitudinal studies of well-nourished women with access to ample food supplies show a slight, although not always statistically significant or universal, increase in energy intake (17). In a group of Scottish women who weighed their food intakes periodically during gestation, total energy intake increased gradually throughout the second and third trimesters so that intakes at parturition were ≈ 0.63 MJ/d (150 kcal/d) higher than was food intake before pregnancy (18). In a similar study of Dutch women, energy intake was unchanged in the first 2 trimesters of pregnancy and increased in the third trimester by ≈ 0.197 MJ/d (47 kcal/d) (19). Minor, but inconsistent, changes in energy intakes were reported in other studies of well-nourished women (20). The substantial variability in food intake that is typical in humans and the cross-sectional design of many of these studies contributed to the reason that no significant changes in food intake were shown.

Food choices

Beliefs about prenatal diets and food cravings or food aversions may influence food choices in pregnant women. It is widely believed by women of all ages, ethnic groups, and income and education levels that the consumption of certain foods marks a child before birth (21). Excess intake of craved foods by pregnant women is thought to explain physical or behavioral peculiarities of infants. Unsatisfied cravings are thought to explain birth marks that mimic the shape of the desired food (eg, strawberry-shaped marks). It is also thought that the mother's consumption of certain foods may cause the child to like those foods.

There is the belief that diet influences ease of delivery. For example, some believe that animal-protein foods and excessive weight gain during pregnancy cause more difficult deliveries. Most pregnant women know that low maternal weight gain will produce a small fetus, which will be delivered more easily than a large fetus. Pregnant women may consciously choose not to consume certain foods during pregnancy for a variety of personal reasons (ie, food avoidances). The foods most commonly avoided by pregnant women are usually good sources of animal protein, such as milk, lean meats, pork, and liver. Food cravings and food aversions are powerful urges to consume or not consume particular foods, respectively. The most common aversions are to alcohol, caffeinated drinks, and meats. Dairy and sweet foods are the most commonly reported craved foods. It is not uncommon for pregnant women to increase their consumption of milk. For example, in a longitudinal study of calcium metabolism, Ritchie et al (16) reported that dietary calcium increased by 300 mg/d between preconception and the third trimester of pregnancy, even though the women were specifically told to not increase their intake of dairy products. This increase in milk consumption also caused a significant increase in dietary zinc (22).

Knowledge of the individual's total dietary intake is necessary before the nutritional effect of food cravings or aversions can be assessed. However, in general, most food cravings cause an increase in calcium and energy intakes, whereas food aversions cause a decrease in intakes of alcohol, caffeine, and animal protein. Food cravings and aversions do not necessarily have a deleterious effect on the quality of the diet.

Physical activity

The energy cost of weight-bearing activity increases in pregnancy because of increases in body weight; however, no allowance is made for this additional energy cost. It is assumed



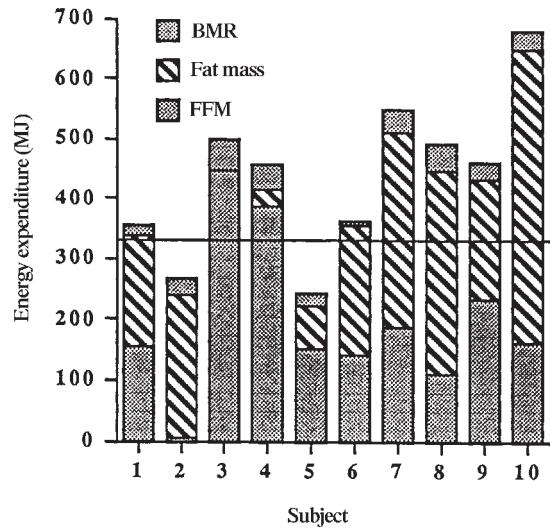


FIGURE 1. Total energy expenditure for the cumulative increase in basal metabolic rate (BMR), fat mass gain, and fat-free mass (FFM) gain during pregnancy in 10 healthy, normal weight women. Total energy cost: 434 ± 132 MJ ($\bar{x} \pm$ SD of the 10 subjects); theoretical energy cost: 336 MJ. From reference 11.

that the increased costs of physical activity are offset by a decrease in the amount of time spent in weight-bearing activities and by the relaxed and economical fashion in which pregnant women move (23, 24). If the pace or intensity of an activity is fixed, the energy cost of non-weight-bearing activities (eg, cycling) does not increase. In absolute terms, energy expenditure associated with sedentary activities such as sitting and standing increases in proportion to the increases in basal metabolism. The absolute cost of weight-bearing activity increases, but the cost of walking on a treadmill per unit body weight does not differ between pregnant and nonpregnant women (17).

Because the energy cost of weight-bearing activity rises in proportion to the increase in body weight, a reduction in those activities during gestation is expected. Generally, there is less walking and more sitting among women in industrialized societies, but the changes are subtle (17). Few studies have specif-

ically examined the activity patterns of pregnant women in developing countries. The available studies show that pregnant women perform the same types of activities as nonpregnant women. However, during the third trimester of pregnancy, particularly in the last month, women spend less time performing strenuous activities (25). Much of the physical activity of women living in rural areas involves bending, walking, and carrying loads; all of these activities are more difficult for pregnant women to engage in. These women typically spend 2–3 h/d gathering water and fuel and preparing food and many perform weight-bearing agricultural activities for an additional 5–10 h/d. Low-income women living in urban areas in developing countries are often as active as those women living in rural areas, but the activities may not be as energy intensive. This high degree of physical activity performed by women in developing countries is not offset by increases in energy intake.

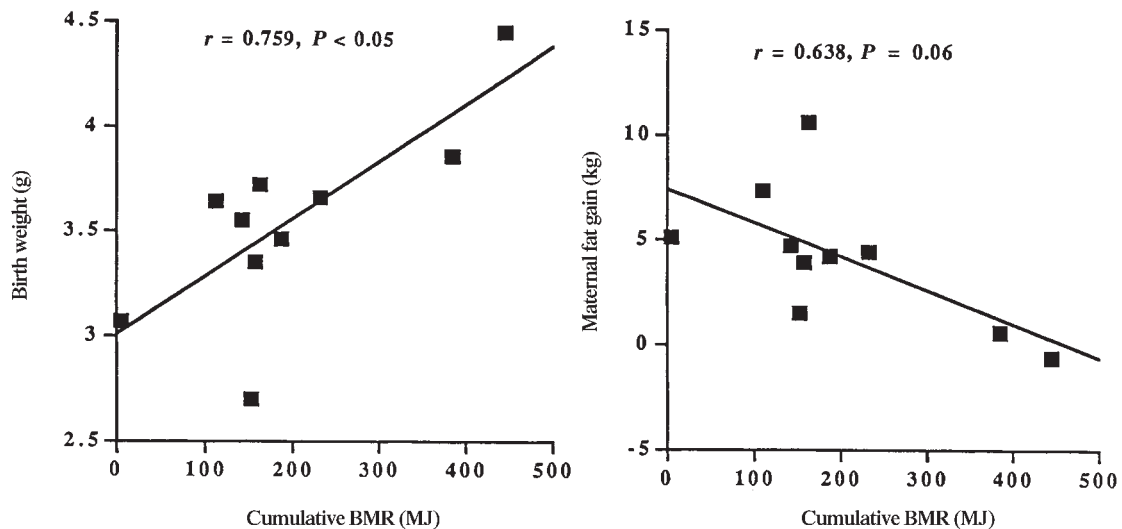


FIGURE 2. Correlation between the cumulative increase in basal metabolic rate (BMR) and birth weight or maternal fat gain. From reference 11.



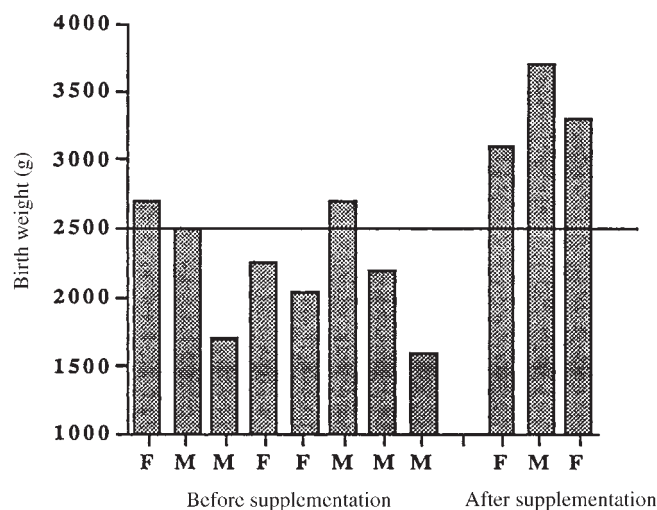


FIGURE 3. Birth weight of 11 children born to a poor woman in Montreal; 8 children were born before receiving nutritional counseling and food supplements from the Montreal Diet Dispensary and 3 children were born afterward. All 3 of the last infants weighed >2500 g, the standard used to define a low-birth-weight baby. Adapted from reference 27.

The resulting imbalance in the energy supply is reflected in low weight gain, impaired fetal growth, and a decreased ability to sustain milk production (25).

If women do not have the option of changing their weight-bearing activities, they may compensate for the extra energy needed to move their heavier bodies by decreasing either their pace or the intensity of the activity. Data show that physical pace decreases in late pregnancy during stair climbing and walking with a 5-kg load, but does not change with light activities such as window washing or sweeping (23, 26). Nagy and King (27) studied the effect of pregnancy on pace by measuring the time required to walk 400 m or climb 6.9 m of stairs during pregnancy. Five women were studied at 15, 25, 30, and 35 wk gestation. No significant differences in pace were noted and the women continued to maintain a pace equivalent to that of nonpregnant women despite a weight gain of 12.7 kg. In contrast, 4 other women at 33 wk gestation walked 20% more slowly than did nonpregnant women. Individual behavior, therefore, seems to have a greater influence on the pace of walking or stair climbing than does the stage of pregnancy. Even though the women were allowed to voluntarily decrease their pace and, consequently, their energy expenditure per minute, they did not do so and the energy cost to complete the task increased in relation to the increase in body weight. The number of women in these studies is small, and it is inappropriate to draw general conclusions from the research. However, it appears that the primary effect of pregnancy on physical activity is mediated through the increase in maternal body weight.

LIMITED ADJUSTMENTS IN NUTRIENT METABOLISM

Although there are multiple potential adjustments for the metabolism of nutrients during pregnancy, a threshold in the capacity to make those adjustments exists. When food intake falls below the threshold, fetal growth and development are reduced, and such women are at greatest risk of poor pregnancy outcomes and will benefit the most from nutritional interventions. This is clearly shown by a case from the files of the Montreal Diet Dispensary (28). Between 1963 and 1972, the


Montreal Diet Dispensary provided nutrition counseling and food supplements to 1736 maternity clinic patients at the Royal Victorian Hospital. Mothers whose incomes were below the poverty level received additional milk, eggs, and oranges. Because these mothers were not accustomed to drinking milk, they were told that they were drinking the milk for the baby, not for themselves. The potential effect of this nutritional intervention on pregnancy outcome in undernourished women is shown by the case of a 29-y-old mother who delivered 11 children at the Royal Victorian Hospital. Eight of the children were born before the woman received food and counseling from the Montreal Diet Dispensary; 3 of the children were born after counseling. All 8 of the children born before counseling were born with health problems; the third child died at the age of 1 mo (**Figure 3**). The 3 children born after the mother received nutritional support from the Montreal Diet Dispensary were healthy and weighed >3 kg.

The nutrient intakes of this woman are not known, but it is clear that the physiologic adjustments made during her first 8 pregnancies were insufficient to meet fetal needs. In other words, her nutrient intakes were below her threshold of pregnancy. The addition of ≈ 2.2 MJ (525 kcal) and 35 g protein improved her nutritional status and her ability to deliver healthy, full-term infants.

The thresholds for nutrient intakes to support good pregnancy outcomes are not fixed values. Instead, they undoubtedly vary widely from woman to woman depending on her prepregnancy nutritional status and health, fetal size, health and lifestyle during gestation, and genetics. However, populations of similar women should have comparable thresholds. Definition of nutrient thresholds for pregnancy will help identify those women in need of dietary intervention and the appropriate amounts of nutrients to provide in nutritional supplements for pregnant women.

CONCLUSION

Pregnancy consists of a series of small, continuous changes that affect the metabolism of all nutrients. Furthermore, pregnancy is only one phase of a woman's reproductive cycle.

Evidence is accumulating that the prepregnancy period is the best time to prepare for the demands of pregnancy. Provision of Women's, Infants', and Children's supplements for 5–7 mo, instead of <2 mo before conception, resulted in a higher birth weight of 131 g and a greater birth length of 0.3 cm (29). Public health policies should be established to ensure good maternal nutrition during all phases of the reproductive cycle—pregnancy, lactation, and postweaning. 

I acknowledge the assistance of Victoria Cohenour in the preparation of the manuscript and am grateful to Michele Bronstein, Wendy Fitch, Lori Kopp, Sonja Lindquist, Deborah Marino, Laura Nagy, Lorrene Ritchie, and the other postdoctoral fellows and doctoral students who assisted with the studies discussed in this review.

REFERENCES

- Hyttén F, Chamberlain G. *Clinical physiology in obstetrics*. Oxford, United Kingdom: Blackwell Scientific Publications, 1980.
- Food and Nutrition Board, Committee on Nutrition of the Mother and Preschool Child. *Laboratory indices of nutritional status in pregnancy*. Washington, DC: National Academy of Sciences, 1978.
- Denne SC, Patel D, Kalhan SC. Leucine kinetics and fuel utilization during a brief fast in human pregnancy. *Metabolism* 1991;40:1249–56.
- Calloway DH. Nitrogen balance during pregnancy. In: Winick M, ed. *Nutrition and fetal development*. Philadelphia: Wiley & Sons, 1974:79–94.
- Naismith DJ. Adaptations in the metabolism of protein during pregnancy and their nutritional implications. *Nutr Rep Int* 1973;7:383–99.
- Marino DD. Protein utilization during early and late human pregnancy. PhD dissertation. University of California, Berkeley, 1983.
- National Research Council. *Recommended dietary allowances*. 9th ed. Washington, DC: National Academy Press, 1980.
- Hiller A, Plazin J, Van Slyke DD. A study of conditions for kjeldahl determinations of nitrogen in proteins. *J Biol Chem* 1948;176:1401–20.
- Kalhan SC. Protein metabolism in pregnancy. *Am J Clin Nutr* 2000;71(suppl):1249S–55S.
- Fitch WL, King JC. Plasma amino acid, glucose, and insulin responses to moderate-protein and high-protein test meals in pregnant, nonpregnant, and gestational diabetic women. *Am J Clin Nutr* 1987;46:243–9.
- King JC, Butte NF, Bronstein MN, Kopp LE, Lindquist SA. Energy metabolism during pregnancy: influence of maternal energy status. *Am J Clin Nutr* 1994;59(suppl):439S–45.
- Kopp-Hoolihan L, van Loan MD, WW Wong, King JC. Longitudinal assessment of energy balance in well-nourished, pregnant women. *Am J Clin Nutr* 1999;69:697–704.
- Poppitt SD, Prentice AM, Jequier E, Schutz Y, Whitehead RG. Evidence of energy sparing in Gambian women during pregnancy: a longitudinal study using whole-body calorimetry. *Am J Clin Nutr* 1993;57:353–64.
- Bronstein MN, Mak RP, King JC. Unexpected relationship between fat mass and basal metabolic rate in overweight pregnant women. *Br J Nutr* 1995;74:261–75.
- Kusin JA, Kardjati S, Houtkooper JM, Renqvist UH. Energy supplementation during pregnancy and postnatal growth. *Lancet* 1992;340:623–6.
- Ritchie LD, Fung EB, Halloran BP, et al. A longitudinal study of calcium homeostasis during human pregnancy and lactation and after resumption of menses. *Am J Clin Nutr* 1998;67:693–701.
- Committee on Maternal Nutrition, Food and Nutrition Board, National Research Council. *Maternal nutrition and the course of pregnancy*. Washington, DC: National Academy of Sciences, 1970.
- Durnin JVGA, McKillop FM, Grant S, Fitzgerald G. Energy requirements of pregnancy in Scotland. *Lancet* 1987;2:897–900.
- van Raaij JMA, Vermaat-Miedema SH, Schonk CM, Peek MEM, Hautvast JGAJ. Energy requirements of pregnancy in the Netherlands. *Lancet* 1987;2:953–5.
- King JC, Bronstein MN, Fitch WL, Weininger J. Nutrient utilization during pregnancy. *World Rev Nutr Diet* 1987;52:71–142.
- Committee on Nutrition of the Mother and Preschool Child, Food and Nutrition Board, National Research Council. *Alternative dietary practices and nutritional abuses in pregnancy*. Washington, DC: National Academy Press, 1982.
- Fung EB, Ritchie LD, Woodhouse LR, Roehl R, King JC. Zinc absorption in women during pregnancy and lactation: a longitudinal study. *Am J Clin Nutr* 1997;66:80–8.
- Blackburn MW, Calloway DH. Basal metabolic rate and work energy expenditure of mature, pregnant women. *J Am Diet Assoc* 1976;69:24–8.
- Banerjee B, Khew KS, Saha N. A comparative study of energy expenditure in some common daily activities of non-pregnant and pregnant Chinese, Malay and Indian women. *J Obstet Gynaecol Br Commonw* 1971;78:113–6.
- Subcommittee on Diet Physical Activity, and Pregnancy Outcome, Committee on International Nutrition Programs, Food and Nutrition Board, Institute of Medicine. *Nutritional issues in developing countries. II. Diet and activity during pregnancy and lactation*. Washington, DC: National Academy Press, 1992.
- Appel J. Protein and energy utilization in pregnant and nonpregnant women. PhD dissertation. University of California, Berkeley, 1980.
- Nagy LE, King JC. Postprandial energy expenditure and respiratory quotient during early and late pregnancy. *Am J Clin Nutr* 1984;40:1258–63.
- Higgins AC. Nutritional status and the outcome of pregnancy. *J Can Diet Assoc* 1976;37:17–35.
- Caan B, Horgen DM, Margen S, King JC, Jewell NP. Benefits associated with WIC supplemental feeding during the interpregnancy interval. *Am J Clin Nutr* 1987;45:29–41.