Adjustments in energy expenditure and substrate utilization during late pregnancy and lactation[1–4]

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ABSTRACT

Background: Metabolic adjustments occur during pregnancy and lactation to support fetal growth and milk synthesis; however, the effect of body composition and hormonal milieu on these changes is poorly understood.

Objective: We hypothesized that energy metabolism changes during pregnancy and lactation to support fetal growth and milk synthesis, and that body composition and hormonal milieu influence these alterations.

Design: We measured energy expenditure, body composition, and hormone, metabolite, and catecholamine concentrations in 76 women (40 lactating, 36 nonlactating) at 37 wk gestation and 3 and 6 mo postpartum. Total energy expenditure (TEE), basal metabolic rate (BMR), sleeping metabolic rate (SMR), and minimal SMR (MSMR) were measured with room calorimetry. Fat-free mass (FFM) and fat mass were estimated with a 4-component model.

Results: TEE, BMR, SMR, and MSMR were 15–26% higher during pregnancy than postpartum after being adjusted for FFM, fat mass, and energy balance. TEE, SMR, and MSMR were higher in lactating than in nonlactating women. Fasting serum insulin, insulin-like growth factor I, fatty acids, and leptin, and 24-h urinary free norepinephrine, epinephrine, and dopamine correlated positively with TEE, BMR, SMR, and MSMR. In nonlactating women, the respiratory quotient decreased over time, carbohydrate oxidation decreased, and fat oxidation increased. Substrate utilization was not influenced by body composition, fasting serum hormones, or 24-h urinary catecholamines.

Conclusions: These results indicate increased energy expenditure and preferential use of carbohydrates during pregnancy and lactation. Elevated respiratory quotient and carbohydrate utilization during pregnancy continue during lactation, consistent with preferential use of glucose by the fetus and mammary gland. *Am J Clin Nutr* 1999;69:299–307.

KEY WORDS Energy expenditure, basal metabolic rate, sleeping metabolic rate, substrate oxidation, pregnancy, lactation, breast-feeding, resting energy expenditure, resting metabolic rate, fat oxidation, lipid oxidation, carbohydrate oxidation, women

INTRODUCTION

Numerous metabolic adjustments occur during pregnancy and lactation to support fetal growth and milk synthesis, respectively, without jeopardizing maternal homeostasis (1). In late gestation, rising concentrations of human chorionic somatomammotropin, prolactin, cortisol, and glucagon exert lipolytic and antiinsulinogenic effects that promote greater utilization of alternative fuels, particularly fatty acids, by peripheral tissues. These metabolic changes ensure that a constant supply of glucose and amino acids reaches the fetus. During lactation, mechanisms develop to promote the preferential utilization of nutrients by the mammary gland (2). Hypoinsulinemia and diminished responsiveness to insulin in adipose and muscle tissue favor uptake of nutrients by the mammary gland.

Although these hormonal changes ensure a uniform flow of nutrients to the fetus and to the mammary gland, their effect on maternal energy metabolism is unclear. During pregnancy, energy expenditure generally rises because of increases in maternal and fetal weight. However, the variability in metabolic response among women is striking (3–5) and has been attributed to differences in body fatness (3, 6). Declines in basal metabolic rate (BMR) and in the energy costs of exercise may indicate energy conservation or augmented metabolic efficiency in some pregnant women (3, 4). Conflicting data have been reported on BMR and resting metabolic rate (RMR) in lactating women, with some authors reporting that it increased (7, 8) and others finding that it remained unchanged (9–11).

During pregnancy, metabolic fuel utilization measured with the use of respiration calorimetry reflects the oxidative contribution of the maternal and fetal compartments. Some investigators have reported increased respiratory quotients in pregnancy, indicating higher rates of net carbohydrate utilization (12, 13), whereas others found no changes in respiratory quotients (14). The respiratory quotient in lactation was lower in one study (7)

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and unchanged in other studies (10, 15). The effects of body composition and hormonal milieu on metabolic responses to pregnancy and lactation have not been investigated thoroughly.

In this study, we examined energy metabolism during late pregnancy and lactation in a group of well-nourished women. We hypothesized that energy metabolism is altered in pregnancy and lactation to support fetal growth and milk synthesis, respectively, and that these alterations are influenced by maternal body composition and hormonal milieu. Energy metabolism was studied by using highly precise room respiration calorimeters and body composition was determined by using a 4-component model validated in pregnant and postpartum women (16, 17). These technical improvements may resolve some of the controversies regarding adaptations in energy metabolism during pregnancy and lactation.

SUBJECTS AND METHODS

Study design

To investigate energy expenditure and substrate utilization during late pregnancy and lactation, longitudinal measurements of energy expenditure (by respiration calorimetry), body composition, fasting serum hormones and metabolites, and 24-h urinary catecholamines were performed in 76 women at 36–38 wk gestation and at 3 and 6 mo postpartum. The women recruited were required to either exclusively breast-feed (n = 40) or exclusively formula-feed (n = 36) their infants from birth to 4 mo of age. Subjects were assigned to 2 groups (L, lactating; NL, nonlactating) according to infant feeding preference. The study design allowed for comparisons among pregnancy, lactation, and the nonpregnant, nonlactating postpartum state. At each study interval, subjects were admitted for 2 d to the Metabolic Research Unit of the Children's Nutrition Research Center in Houston.

Subjects

To be eligible, subjects had to be 18–35 y of age with parity ≤4, have no known medical conditions, have no obstetric complications, and not smoke or abuse substances. Prepregnancy body mass index (BMI; in kg/m^2), derived from subject recall of weight and height, was <30. The subjects' obstetricians confirmed that their health histories and pregnancies were unremarkable.

The mean (±SD) age of the 76 women was 28.8 ± 4.2 y; there were 55 whites, 7 African Americans, 11 Hispanics, and 3 Asians. Median gravidity and parity were 2 (range: 1–5) and 0 (range: 0–3), respectively. Gestational weight gain was 16.2 ± 5.3 kg. All the women gave birth to healthy, full-term infants with a mean gestational age of 39.1 ± 1.3 wk, birth weight of 3.4 ± 0.4 kg, and birth length of 50.6 ± 2.2 cm. The above characteristics did not differ significantly between the L and NL groups. Respiration calorimetry results were available for 205 of the 228 scheduled visits. Subject data were missing due to delivery before the scheduled visit (n = 4), enrollment after delivery (n = 5), subsequent pregnancy (n = 1), and subject scheduling conflicts (n = 5). In addition, 8 women who discontinued breast-feeding between 4 and 6 mo were eliminated from the analysis at 6 mo because one of the study aims was to investigate the effect of lactation on energy metabolism. The milk production of the remaining 32 lactating women provided 76 ± 29% of the infants' energy needs. The study was approved by the Baylor Affiliates Review Board for Human Subject Research. Written, informed consent was obtained from the subjects for all studies.

Body-composition measurements

Body weight and height were measured with an electronic balance (Healthometer, Bridgeview, IL) and stadiometer (Holtain Limited, Croswell, Crymych, United Kingdom), respectively. The Fuller et al (18) 4-component model—based on body weight, total body water (TBW), body volume, and bone mineral content (BMC)—was used to estimate fat-free mass (FFM) and fat mass. In pregnancy, simpler 2-component models are invalid because of the increased hydration of FFM. The 4-component model, although valid in pregnancy (16), does not distinguish between maternal and fetal tissues. TBW was determined by dilution of an orally administered dose of deuterium oxide (40 or 100 mg ^2H_2O/kg) (19). Baseline and postdose saliva samples were collected; postdose samples were obtained at 4 and 6 h, or daily for 14 d. The higher dose and longer sampling period were used as part of the doubly labeled water method, for estimation of total energy expenditure (TEE), in a subset of pregnant women at 37 wk gestation and in lactating women at 3 mo postpartum (unpublished observations).

Before analysis, hydrogen gas was generated from undistilled saliva samples by zinc reduction in quartz vessels. Deuterium abundance in saliva samples was measured by gas isotope ratio mass spectrometry (Delta-E; Finnigan MAT, San Jose, CA). Deuterium dilution space was calculated from the average of the 4- and 6-h postdose saliva samples by the plateau method, or from the 14 daily saliva samples by extrapolation, and was converted to TBW by dividing by 1.04. Body volume was measured with an underwater weighing system using "force cube" transducers (Precision Biomedical Systems, Inc, State College, PA) (20). Body volume was corrected for residual lung volume measured with the simplified nitrogen washout method immediately before underwater weighing (21). Subjects were instructed to exhale maximally for measurements of residual lung volume and body volume. Dual-energy X-ray absorptiometry (software version 5.56, QDR2000; Hologic, Inc, Madison, WI) was used to measure total-body BMC. Fat mass was estimated from body weight, TBW, body volume, and BMC by using the Fuller et al (18) 4-component model:

$$\text{Fat mass} = 2.747\ \text{body volume} - 0.71\ \text{TBW} + 1.46\ \text{BMC} - 2.05\ \text{wt} \quad (1)$$

where fat mass is in kg, body volume is in L, TBW is in L, BMC is in kg, and wt is body weight in kg. To avoid radiation exposure during pregnancy, BMC was measured 0.5 mo after delivery. FFM was computed as the difference between body weight and fat mass.

Room respiration calorimetry

Oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), and respiratory quotient ($\dot{V}CO_2/\dot{V}O_2$) were measured continuously in 31-m^3 room calorimeters for 24 h. The performance of the respiration calorimeters was described in detail previously (22). Calorimeter temperature and relative humidity averaged 23.7 ± 0.6 °C and 43.0 ± 5.6%, respectively. Heart rate was recorded by telemetry (DS-3000; Fukuda Denshi, Tokyo) and physical activity was monitored by a Doppler microwave sensor

TABLE 1
Anthropometry and body composition of subjects at 37 wk gestation and 3 and 6 mo postpartum[1]

	Pregnancy		3 mo postpartum		6 mo postpartum		*P* (ANOVA)		
	L (n = 38)	NL (n = 29)	L (n = 39)	NL (n = 35)	L (n = 32)	NL (n = 32)	Feeding mode	Time	Feeding mode × time
Weight (kg)	75.5 ± 9.7[2]	74.9 ± 11.8	65.5 ± 11.0	64.1 ± 10.3	62.7 ± 10.0	63.9 ± 11.6	NS	0.001	NS
Height (cm)	164.3 ± 6.1	163.2 ± 5.8	—	—	—	—			
BMI	28.0 ± 3.6	28.2 ± 4.2	24.3 ± 3.9	24.1 ± 3.8	23.2 ± 3.7	24.2 ± 4.3	NS	0.001	NS
FFM (kg)	52.7 ± 5.2	51.2 ± 5.9	43.8 ± 5.2	42.7 ± 5.0	43.7 ± 4.6	42.4 ± 5.3	NS	0.001	NS
Fat mass									
(kg)	22.8 ± 6.8	23.8 ± 7.8	21.7 ± 8.0	21.4 ± 7.5	19.0 ± 10.6	21.6 ± 8.5	NS	0.001	NS
(%)	29.7 ± 5.7	31.0 ± 6.3	32.2 ± 7.4	32.6 ± 6.8	29.3 ± 8.0	32.8 ± 7.6	NS	0.001	NS

[1] L, lactating; NL, nonlactating; FFM, fat-free mass.
[2] $\bar{x}$ ± SD.

with output in counts (D9/50; Microwave Sensors, Ann Arbor, MI). A 24-h urine collection was obtained for nitrogen and catecholamine determinations while the subjects were in the calorimeter. TEE, nonprotein energy expenditure (NPEE), and net substrate utilization were computed from the 24-h $\dot{V}O_2$, $\dot{V}CO_2$, and urinary nitrogen excretion data according to the method described by Livesey and Elia (23). Net energy balance was computed as energy intake minus TEE. In lactating women, TEE included the energy expended for milk synthesis but not the energy content of the milk.

The subjects adhered to a schedule while in the calorimeter. Calorimetry began at 0800. Meals were served at 0830, 1200, and 1730, with a snack at 1830. A set menu was adjusted to provide 1.3 times the subject's predicted BMR, based on her age and weight (24), with an additional allowance for pregnancy (1255 kJ) or lactation (2092 kJ). The diet provided 50% of energy from carbohydrate, 30% from fat, and 20% from protein, with a corresponding food quotient of 0.875. The subjects exercised for 15 min once in the morning and once in the afternoon by walking on a treadmill at 3.2 km/h, at no grade (905E; Precor, Bothell, WA). At 1600, the women were asked to take a 1.5-h nap. For the rest of the day, the subjects were allowed free choice of sedentary activities (such as reading, writing, or watching television). No food was allowed after 1900, and bedtime was at 2200. Sleeping metabolic rate (SMR) was defined as the mean energy expenditure during all nighttime sleeping, with sleep confirmed by physical activity and heart rate monitors. Minimal SMR (MSMR) was the lowest energy expenditure observed for 20 consecutive minutes of sleep. At 0700, subjects were awakened and remained supine for 40 min for the measurement of BMR. A fasting blood sample was obtained when each subject exited the calorimeter.

Milk production

All milk produced during the 24 h in the calorimeter was expressed with an electric breast pump. After each pumping session, the milk was weighed and a 10% aliquot was refrigerated and later pooled for analysis; the remainder was fed to the infant. Milk was analyzed for energy content by adiabatic bomb calorimetry (Parr Instruments, Moline, IL).

Hormones, metabolites, and catecholamines

Radioimmunoassays were used to measure insulin, glucagon, cortisol, dehydroepiandrosterone sulfate (DHEAS), and prolactin (Diagnostics Product Corp, Los Angeles) concentrations, and insulin-like growth factor I (IGF-I) (Nichols Institute, San Juan Capistrano, CA). Serum leptin was measured with a solid-phase sandwich enzyme immunoassay by using an affinity-purified polyvalent antibody raised against recombinant human leptin. Serum glucose, triacylglycerol, and fatty acids and urinary creatinine were determined enzymatically with a Cobas-Bio automated instrument (Roche Diagnostic Systems, Nutley, NJ). Urinary cortisol was determined by radioimmunoassay after extraction with dichloromethane. Urinary excretion of norepinephrine, epinephrine, and dopamine was measured by HPLC. Catecholamines were extracted with a cation exchange column, separated by reversed-phase chromatography (model no. 126; Beckman Instruments, Inc, San Ramon, CA), and detected with an electrochemical detector (model LC-4B; BioAnalytical Systems, West Lafayette, IN). Urinary nitrogen was determined by the Kjeldahl technique (Kjeltec Auto Analyzer 1030; Tecator, Hoganas, Sweden).

Statistical analysis

The data are reported as means ± SDs. Descriptive statistics, correlations, and multiple regression analyses were performed by using MINITAB (release 12; Minitab, Inc, State College, PA). Repeated-measures analysis of variance (ANOVA) with time-varying covariates (5V; BMDP Statistical Software, Inc, Los Angeles) was used to test the effects of pregnancy and lactation on energy expenditure and substrate utilization. The basic model included a grouping factor (L or NL), a time factor (37 wk gestation, 3 mo postpartum, or 6 mo postpartum), covariates (FFM, fat mass, and net energy balance), and an interaction between group and time. Significant interactions were examined further by reanalyzing the effect of time (37 wk gestation, 3 mo postpartum, or 6 mo postpartum) within a group with repeated-measures ANOVA and by making comparisons between L and NL with one-way ANOVA. In addition, hormones, metabolites, and catecholamines were added as time-varying covariates to the basic model to test their effects on rates of energy expenditure and substrate utilization.

RESULTS

Body composition, fasting serum hormones and metabolites, and 24-h urinary catecholamines

Anthropometric and body-composition measurements did not differ significantly between the L and NL groups (**Table 1**). Weight, FFM, and fat mass decreased over time (P = 0.001) in the L and NL groups. Fasting serum hormones and metabolites

TABLE 2
Fasting serum hormone and metabolite concentrations of subjects at 37 wk gestation and 3 and 6 mo postpartum[1]

	Pregnancy		3 mo postpartum		6 mo postpartum		*P* (ANOVA)		
	L (n = 38)	NL (n = 29)	L (n = 39)	NL (n = 35)	L (n = 32)	NL (n = 32)	Feeding mode	Time	Feeding mode × time
Insulin (pmol/L)	64 ± 23[2]	69 ± 33	46 ± 21	70 ± 22	55 ± 25	73 ± 27	0.008	0.02	0.008
Glucose (mmol/L)	4.0 ± 0.4	4.0 ± 0.3	4.5 ± 0.4	4.7 ± 0.4	4.6 ± 0.4	4.7 ± 0.4	0.04	0.001	NS
Insulin:glucose	16 ± 6	17 ± 8	10 ± 5	15 ± 5	12 ± 6	15 ± 5	0.005	0.001	0.04
Glucagon (ng/L)	159 ± 40	165 ± 27	81 ± 43	136 ± 46	83 ± 53	139 ± 47	0.001	0.001	0.001
IGF-I (μg/L)	395 ± 102	415 ± 194	230 ± 50	254 ± 67	266 ± 75	286 ± 81	NS	0.001	NS
Cortisol (nmol/L)	1042 ± 212	1007 ± 216	463 ± 142	586 ± 273	455 ± 133	574 ± 278	0.01	0.001	0.01
DHEAS (μmol/L)	2.9 ± 1.2	2.9 ± 1.1	4.9 ± 2.3	3.1 ± 1.6	4.6± 2.2	3.5 ± 1.9	0.007	0.001	0.001
Leptin (μg/L)	29 ± 18	31 ± 16	16 ± 16	20 ± 14	15 ± 14	20 ± 15	NS	0.001	NS
Prolactin (μg/L)	251 ± 89	233 ± 74	85 ± 55	12 ± 6	37 ± 22	13 ± 9	0.001	0.001	0.001
Triacylglycerol (mmol/L)	3.25 ± 1.11	3.22 ± 0.96	1.05 ± 0.40	1.67 ± 0.56	1.16 ± 0.55	1.68 ± 0.65	0.003	0.001	0.001
Fatty acids (mmol/L)	0.84 ± 0.30	0.71 ± 0.23	0.76 ± 0.34	0.60 ± 0.21	0.79 ± 0.33	0.58 ± 0.22	0.001	0.03	NS

[1] L, lactating; NL, nonlactating; IGF-I, insulin-like growth factor I; DHEAS, dehydroepiandrosterone sulfate.
[2] $\bar{x}$ ± SD.

are summarized in **Table 2**. Serum glucose was lower in pregnancy than postpartum in both groups. IGF-I and leptin concentrations were higher during pregnancy than postpartum in both groups. Several significant interactions between feeding mode (L or NL) and time occurred, requiring further analysis. Serum insulin was significantly lower in the L than in the NL group at 3 and 6 mo postpartum (P = 0.001). Insulin resistance occurred during pregnancy, as indicated by the insulin-glucose ratio, which was higher at 37 wk gestation than during the postpartum period. Lower insulin-glucose ratios were observed in the L than in the NL group postpartum (P = 0.01). Serum glucagon, cortisol, and triacylglycerol were significantly higher during pregnancy than postpartum, and were significantly lower in the L than in the NL group postpartum. DHEAS was elevated postpartum in the L group only. Prolactin was higher during pregnancy than postpartum and was higher in the L than in the NL group postpartum.

The data for 24-h urinary excretion of catecholamines and cortisol at 37 wk gestation and 3 and 6 mo postpartum are presented in **Table 3**. Excretion of free norepinephrine differed over time, with higher excretion during pregnancy; this occurred when free norepinephrine was and was not corrected for urinary creatinine. For free epinephrine, both corrected and uncorrected for urinary creatinine, significant feeding mode and time effects occurred. Excretion of free epinephrine was higher postpartum and was higher in the L than in the NL group at 37 wk gestation and 3 and 6 mo postpartum. Free dopamine was higher during pregnancy than postpartum. When corrected for creatinine, free dopamine was lower in the L than in the NL group at 37 wk gestation (P = 0.001), 3 mo postpartum (P = 0.04), and 6 mo postpartum (P = 0.05). When corrected or uncorrected for creatinine, excretion of cortisol was higher during pregnancy than postpartum. When corrected for creatinine, cortisol excretion did not differ significantly between the L and the NL groups.

Total energy expenditure

Results of the calorimetric determinations are presented in **Tables 4** and **5** and **Figure 1**. Mean $\dot{V}O_2$, $\dot{V}CO_2$, respiratory quotient, energy expenditure, heart rate, and physical activity are

TABLE 3
24-h Urinary excretion of catecholamines and cortisol of subjects at 37 wk gestation, and 3 and 6 mo postpartum[1]

	Pregnancy		3 mo postpartum		6 mo postpartum		*P* (ANOVA)		
	L (n = 38)	NL (n = 29)	L (n = 39)	NL (n = 35)	L (n = 32)	NL (n = 32)	Feeding mode	Time	Feeding mode × time
24-h Free NE (nmol/d)	206 ± 68[2]	199 ± 94	134 ± 37	132 ± 50	146 ±41	150 ± 54	NS	0.001	NS
24-h Free E (nmol/d)	16 ± 6	11 ± 5	17 ± 8	11 ± 6	18 ± 9	14 ± 7	0.001	0.001	NS
24-h Free DA (nmol/d)	1581 ± 406	1770 ± 518	1252 ± 376	1348 ± 479	1287 ± 436	1388 ± 468	NS	0.001	NS
24-h Total NE (nmol/d)	1916 ± 783	1476 ± 752	1321 ± 518	787 ± 293	1202 ± 436	872 ± 331	0.001	0.001	NS
24-h Total E (nmol/d)	57 ± 22	39 ± 22	48 ± 25	30 ± 14	59 ± 29	38 ± 19	0.001	0.001	NS
24-h Total DA (nmol/d)	24317 ± 7205	18780 ± 6789	20912 ± 8540	12491 ± 4591	20690 ± 6031	12414 ± 5095	0.001	0.001	NS
Free NE:creatinine (nmol/mmol)	18 ± 7	21 ± 12	13 ± 4	14 ± 6	15 ± 4	17 ± 6	NS	0.001	NS
Free E:creatinine (nmol/mmol)	1.4 ± 0.6	1.2 ± 0.7	1.7 ± 0.9	1.2 ± 0.7	1.9 ± 1.1	1.6 ± 0.8	0.02	0.001	NS
Free DA:creatinine (nmol/mmol)	140 ± 31	186 ± 73	124 ± 34	147 ± 60	131 ± 32	159 ± 64	0.001	0.001	0.01
Total NE:creatinine (nmol/mmol)	172 ± 70	150 ± 78	131 ± 47	85 ± 32	122 ± 40	96 ± 31	0.001	0.001	NS
Total E:creatinine (nmol/mmol)	5.1 ± 2.1	4.1 ± 2.8	4.8 ± 2.5	3.2 ± 1.5	6.2 ± 3.3	4.2 ± 1.8	0.001	0.001	NS
Total DA:creatinine (nmol/mmol)	2172 ± 623	1951 ± 950	2091 ± 896	1340 ± 497	2146 ± 719	1388 ± 563	0.001	0.001	0.02
24-h Total cortisol (nmol/d)	747 ± 213	646 ± 191	270 ± 67	215 ± 69	317 ± 162	242 ± 100	0.001	0.001	NS
Cortisol:creatinine (nmol/mmol)	66 ± 18	68 ± 31	27 ± 7	23 ± 8	32 ± 11	27 ± 11	NS	0.001	NS

[1] L, lactating; NL, nonlactating; NE, norepinephrine; E, epinephrine; DA, dopamine.
[2] $\bar{x}$ ± SD.

TABLE 4
Total energy expenditure (TEE) and basal metabolic rate (BMR) of subjects at 37 wk gestation and 3 and 6 mo postpartum[1]

	Pregnancy		3 mo postpartum		6 mo postpartum		*P* (ANOVA)		
	L (n = 38)	NL (n = 29)	L (n = 39)	NL (n = 35)	L (n = 32)	NL (n = 32)	Feeding mode	Time	Feeding mode × time
TEE									
$\dot{V}O_2$ (L/min)	0.329 ± 0.032[3]	0.316 ± 0.041	0.269 ± 0.030	0.246 ± 0.024	0.258 ± 0.033	0.248 ± 0.029	0.01	0.001	NS
$\dot{V}CO_2$ (L/min)	0.290 ± 0.026	0.279 ± 0.033	0.235 ± 0.027	0.214 ± 0.020	0.227 ± 0.024	0.214 ± 0.020	0.004	0.001	NS
RQ	0.882 ± 0.019	0.885 ± 0.019	0.872 ± 0.024	0.874 ± 0.028	0.876 ± 0.024	0.866 ± 0.023	NS	0.01	0.05
EE (kJ/min)	6.69 ± 0.63	6.44 ± 0.80	5.48 ± 0.58	5.31 ± 0.63	5.31 ± 0.63	5.06 ± 0.58	0.009	0.001	NS
HR (beats/min)	82 ± 11	85 ± 10	67 ± 9	70 ± 10	68 ± 9	73 ± 9	0.01	0.001	NS
Activity (counts)	150 ± 39	122 ± 23	136 ± 26	104 ± 25	125 ± 27	93 ± 18	0.001	0.001	NS
BMR									
$\dot{V}O_2$ (L/min)	0.251 ± 0.028	0.245 ± 0.036	0.202 ± 0.025	0.192 ± 0.020	0.198 ± 0.027	0.191 ± 0.021	NS	0.001	NS
$\dot{V}CO_2$ (L/min)	0.208 ± 0.022	0.208 ± 0.028	0.162 ± 0.020	0.156 ± 0.017	0.159 ± 0.020	0.153 ± 0.018	NS	0.001	NS
RQ	0.828 ± 0.032	0.844 ± 0.043	0.802 ± 0.042	0.808 ± 0.051	0.789 ± 0.042	0.801 ± 0.046	NS	0.001	NS
EE (kJ/min)	5.10 ± 0.54	5.02 ± 0.71	4.08 ± 0.50	3.89 ± 0.38	3.97 ± 0.50	3.85 ± 0.42	NS	0.001	NS
HR (beats/min)	76 ± 11	81 ± 12	58 ± 9	66 ± 13	60 ± 9	69 ± 10	0.001	0.001	NS
Activity (counts/min)	6 ± 9	4 ± 5	5 ± 10	8 ± 15	4 ± 5	5 ± 11	NS	NS	NS
24-h EE:BMR	1.33 ± 0.06	1.30 ± 0.05	1.36 ± 0.08	1.29 ± 0.08	1.31 ± 0.07	1.30 ± 0.06	0.002	NS	NS

[1]L, lactating; NL, nonlactating; RQ, respiratory quotient; EE, energy expenditure; HR, heart rate; $\dot{V}O_2$, oxygen consumption; $\dot{V}CO_2$, carbon dioxide production.
[2]Repeated measures ANOVA, adjusted for fat free mass, fat mass, and net energy balance, and activity in the case of TEE.
[3]$\bar{X}$ ± SD.

presented for TEE, BMR, SMR, and MSMR. TEE was significantly higher during pregnancy than at 3 and 6 mo postpartum. Maternal weight accounted for 59–64% of the variability in TEE.

When the effect of body composition on TEE was tested, both FFM and fat mass had significant effects (P = 0.001). FFM alone accounted for 56%, 62%, and 66% of the variation in TEE at 37 wk gestation, 3 mo postpartum, and 6 mo postpartum, respectively. The addition of fat mass augmented the r^2 value as shown below:

37 wk gestation (r^2 = 68%): TEE = 2177 + 116FFM + 53.5fat mass (*2*)
3 mo postpartum (r^2 = 68%): TEE = 3351 – 555 feeding mode + 101FFM + 28fat mass (*3*)
6 mo postpartum (r^2 = 74%): TEE = 1816 – 195 feeding mode + 121FFM + 30.9fat mass (*4*)

where TEE is in kJ/d, FFM and fat mass are in kg, and feeding mode is coded 1 for L and 2 for NL.

TEE was 15–18% higher during pregnancy than in the postpartum period after adjustment for the significant effects of FFM, fat mass, net energy balance, and activity; adjusted TEE was 6.28, 5.40, and 5.36 kJ/min at 37 wk gestation, 3 mo postpartum, and 6 mo postpartum, respectively. Postpartum values for adjusted TEE were 4–5% higher in the L than in the NL group. Net energy balance differed over time (1.1 MJ/d during pregnancy compared with 0.28 MJ/d postpartum), but not by feeding mode. Heart rate, 24-h activity, and TEE:BMR were higher in the L than in the NL group at all times. After the significantly higher TEE value in the L than in the NL group during pregnancy was controlled for, TEE was higher in the L than in the NL group at 3 and 6 mo postpartum (P = 0.04).

Birth weight correlated positively with TEE during pregnancy (r = 0.41, P = 0.001). When entered as a proxy for fetal weight, birth weight contributed independently to the variation in gestational TEE after FFM and fat mass were controlled for. Addition of birth weight to the model increased the r^2 to 69.4%. Milk energy output (2167 ± 611 kJ/d at 3 mo and 1920 ± 736 kJ/d at 6 mo) correlated positively with TEE postpartum (r = 0.33 at 3 mo and 0.30 at 6 mo, P < 0.02 for both). Addition of milk energy output to the model at 3 and 6 mo postpartum increased the r^2 value to 71.2% and 77.5%, respectively.

Basal metabolic rate

BMR represented 76%, 76%, and 77% of TEE at 37 wk gestation, 3 mo postpartum, and 6 mo postpartum, respectively. In the model in which FFM, fat mass, and net energy balance were adjusted for, BMR differed significantly over time (P = 0.001). Adjusted BMR was 18–20% higher during pregnancy than postpartum (4.83, 4.06, and 4.10 kJ/min at 37 wk gestation, 3 mo postpartum, and 6 mo postpartum, respectively). BMR tended to be higher in the L than in the NL group at 3 mo (P = 0.06) and at 6 mo (P = 0.09) postpartum. Respiratory quotient during BMR measurement was significantly higher during pregnancy than postpartum (time effect: P = 0.001) and was unaffected by covariates.

Sleeping metabolic rate

SMR—adjusted for FFM, fat mass, and net energy balance—was 19–23% higher during pregnancy than postpartum (P = 0.001). After the significantly higher SMR in the L than in the NL group during pregnancy was controlled for, SMR was higher in the L than in the NL group postpartum (P = 0.03). Respiratory quotient during SMR measurement was higher in pregnancy than postpartum, and remained higher during pregnancy (P = 0.001) after adjustment for the significant effect of net energy balance.

Minimal sleeping metabolic rate

MSMR was 5%, 8%, and 8% lower than BMR at 37 wk gestation, 3 mo postpartum, and 6 mo postpartum, respectively. MSMR—adjusted for FFM, fat mass, and net energy balance—was 18–26% higher at 37 wk gestation than during the postpartum period. MSMR was higher in the L than in the NL group at 3 mo

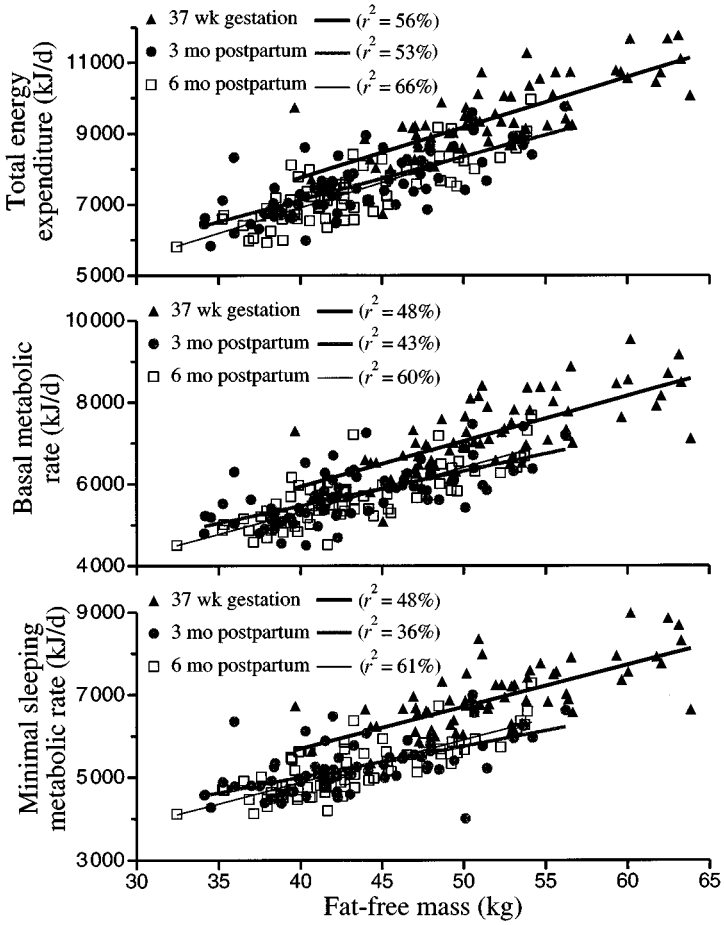

FIGURE 1. Linear relation of total energy expenditure, basal metabolic rate, and minimal sleeping metabolic rate to fat-free mass at 37 wk gestation, 3 mo postpartum, and 6 mo postpartum.

postpartum (P = 0.001). Respiratory quotient during MSMR measurement was higher during pregnancy than postpartum (P = 0.001).

Energy expenditure, fasting serum hormones and metabolites, and 24-h urinary catecholamines

Insulin (P = 0.015–0.076), IGF-I (P = 0.001–0.009), fatty acids (P = 0.001–0.012), leptin (P = 0.007–0.043), free norepinephrine (P = 0.001–0.035), free epinephrine (P = 0.012–0.05), and free dopamine (P = 0.001) were positively correlated with TEE, BMR, SMR, and MSMR after adjustment for FFM, fat mass, and net energy balance in the repeated-measures ANOVA. Urinary total norepinephrine and epinephrine correlated positively with TEE and SMR only (P = 0.01–0.04). DHEAS correlated positively with TEE, BMR, SMR, and MSMR during the postpartum period only (P = 0.005–0.01).

Net substrate utilization

In the repeated-measures ANOVA model, 24-h respiratory quotient was significantly influenced by net energy balance (r = 0.24–0.47, P = 0.001–0.04), but not by FFM or fat mass. The 24-h respiratory quotient declined linearly with time (P = 0.05) in the NL group (adjusted respiratory quotient = 0.886, 0.878, and 0.865 at 37 wk gestation, 3 mo postpartum, and 6 mo postpartum, respectively), resulting in a significant difference between 37 wk gestation and 6 mo postpartum (P = 0.006). In the L group, the 24-h respiratory quotient did not change with time (adjusted respiratory quotient = 0.880, 0.874, and 0.876 at 37 wk gestation, 3 mo postpartum, and 6 mo postpartum, respectively; P = 0.97). The 24-h respiratory quotient differed significantly between groups at 6 mo postpartum (P = 0.05). When adjusted for FFM, fat mass, and energy balance, the nonprotein respiratory quotient (NPRQ) decreased linearly with time in the NL group (adjusted NPRQ = 0.895, 0.887, and 0.872 at 37 wk gestation, 3 mo postpartum, and 6 mo postpartum, respectively; P = 0.02), but not in the L group (adjusted NPRQ = 0.888, 0.884, and 0.887 at 37 wk gestation, 3 mo postpartum, and 6 mo postpartum, respectively).

Rates of net substrate utilization are summarized in **Table 6**. Protein oxidation as a percentage of TEE was significantly lower during pregnancy than postpartum (P = 0.004), and significantly higher in the L than in the NL group (P = 0.001). Over time from 37 wk gestation to 6 mo postpartum, carbohydrate oxidation (% of TEE) decreased linearly (P = 0.006) and fat oxidation (% of TEE) increased linearly (P = 0.008) in the NL group. Carbohydrate oxidation as a percentage of (NPEE) decreased linearly in the NL group, and when adjusted for FFM, fat mass, and energy balance, fell from 66% at 37 wk gestation to 63% and 58% at 3 and 6 mo postpartum, respectively (P = 0.02). Adjusted rates of carbohydrate oxidation averaged 282, 226, and 216 g/d in the L group, and 283, 219, and 204 g/d in the NL group at 37 wk gestation and 3 and 6 mo postpartum,

TABLE 5
Sleeping metabolic rate (SMR) and minimal SMR (MSMR) of subjects at 37 wk gestation and 3 and 6 mo postpartum[1]

	Pregnancy		3 mo postpartum		6 mo postpartum		*P* (ANOVA)		
	L (n = 38)	NL (n = 29)	L (n = 39)	NL (n = 35)	L (n = 32)	NL (n = 32)	Feeding mode	Time	Feeding mode × Time
SMR									
$\dot{V}O_2$ (L/min)	0.252 ± 0.026*	0.246 ± 0.033	0.198 ± 0.023	0.184 ± 0.018	0.194 ±0.025	0.187 ± 0.022	NS	0.001	0.03
$\dot{V}CO_2$ (L/min)	0.219 ± 0.020	0.214 ± 0.026	0.167 ± 0.019	0.156 ± 0.014	0.163 ± 0.020	0.157 ± 0.018	NS	0.001	0.004
RQ	0.867 ± 0.024	0.872 ± 0.030	0.843 ± 0.027	0.848 ± 0.036	0.843 ± 0.025	0.836 ± 0.025	NS	0.001	NS
EE (kJ/min)	5.18 ± 0.51	5.05 ± 0.66	4.04 ± 0.46	3.76 ± 0.37	3.95 ± 0.50	3.82 ± 0.44	0.03	0.001	NS
HR (beats/min)	73 ± 10	77 ± 10	58 ± 9	63 ± 10	60 ± 9	66 ± 9	0.002	0.001	0.007
Activity (counts)	15 ± 10	21 ± 29	11 ± 5	8 ± 5	4 ± 4	3 ± 2	NS	0.001	NS
MSMR									
$\dot{V}O_2$ (L/min)	0.236 ± 0.025	0.231 ± 0.032	0.186 ± 0.022	0.170 ± 0.020	0.180 ± 0.025	0.175 ± 0.019	NS	0.001	NS
$\dot{V}CO_2$ (L/min)	0.206 ± 0.019	0.202 ± 0.026	0.156 ± 0.020	0.146 ± 0.015	0.152 ± 0.021	0.146 ± 0.016	NS	0.001	NS
RQ	0.875 ± 0.038	0.874 ± 0.040	0.835 ± 0.036	0.850 ± 0.049	0.837 ± 0.039	0.839 ± 0.032	NS	0.001	NS
EE (kJ/min)	4.85 ± 0.50	4.77 ± 0.63	3.81 ± 0.46	3.47 ± 0.38	3.64 ± 0.46	3.56 ± 0.38	0.015	0.001	0.01
HR (beats/min)	72 ± 11	76 ± 10	56 ± 9	62 ± 10	57 ± 9	65 ± 9	0.002	0.001	NS
Activity (counts/min)	5 ± 5	5 ± 7	3 ± 7	3 ± 5	2 ± 3	3 ± 3	NS	0.001	NS
BMR:MSMR	1.05 ± 0.05	1.06 ± 0.05	1.07 ± 0.05	1.13 ± 0.10	1.10 ± 0.06	1.08 ± 0.06	NS	NS	NS

[1] L, lactating; NL, nonlactating; RQ, respiratory quotient; EE, energy expenditure, HR, heart rate; BMR, basal metabolic rate; $\dot{V}O_2$, oxygen consumption; $\dot{V}CO_2$, carbon dioxide production.
[2] Repeated-measures ANOVA, adjusted for fat-free mass, fat mass, and net energy balance.
[3] $\bar{x}$ ± SD.

respectively. Conversely, adjusted rates of fat oxidation (% of NPEE) increased over time: 34%, 37%, and 42% in the NL group at 37 wk gestation and 3 and 6 mo postpartum, respectively. Rates of carbohydrate and fat oxidation did not change over time in the L group and were significantly different between groups at 6 mo postpartum (P = 0.03).

Carbohydrate oxidation (% of TEE and % of NPEE) correlated positively with net energy balance, and fat oxidation (% of TEE and % of NPEE) correlated negatively with net energy balance (P = 0.001–0.03). Although the absolute amounts (g/d) of protein, carbohydrate, and fat oxidized were significantly associated with FFM, fat mass (kg), and fat mass (%) (P = 0.001–0.006), oxidation rates (% of TEE or % of NPEE) were not significantly influenced by body composition [FFM, fat mass (kg), or fat mass (%)], fasting serum hormones, or 24-h urinary catecholamines. Fasting serum concentrations of fatty acids were positively associated with fat oxidation and negatively associated with carbohydrate oxidation (g/d, % of TEE, % of NPEE) (P = 0.001–0.01).

DISCUSSION

Energy expenditure during pregnancy (37 wk gestation) and lactation was influenced by body composition and hormonal milieu. Increased rates of energy expenditure and preferential use of carbohydrate were evident during both pregnancy and lactation. TEE and its components, BMR, SMR, and MSMR, were 15–26% higher during pregnancy than in the postpartum period after differences in FFM, fat mass, and net energy balance were adjusted for. The fetus contributed to the hypermetabolism, but increased sympathetic nervous system activity, IGF-I, and leptin may have also played a role. TEE, SMR, and MSMR were elevated during lactation, most likely because of the energy cost of milk synthesis and possibly because of heightened sympathetic nervous system and adrenal activity. The higher respiratory quotient, NPRQ, and net carbohydrate utilization measured in pregnancy were sustained through lactation, which is consistent with the preferential use of glucose by the fetus and mammary gland.

Energy expenditure during pregnancy

Energy expenditure increases during pregnancy because of the metabolic contribution of the uterus and fetus and the increased

TABLE 6
Net substrate utilization determined by respiration calorimetry at 37 wk gestation, and 3 and 6 mo postpartum[1]

	Pregnancy		3 mo postpartum		6 mo postpartum		*P* (ANOVA)[2]		
	L (n = 38)	NL (n = 29)	L (n = 39)	NL (n = 35)	L (n = 32)	NL (n = 32)	Feeding mode	Time	Feeding mode × Time
Protein oxidation (% of TEE)	16 ± 3	14 ± 2	20 ± 3	16 ± 3	21 ± 3	16 ± 4	0.001	0.001	0.03
Carbohydrate oxidation (% of TEE)	54 ± 6	56 ± 6	49 ± 8	51 ± 10	50 ± 8	47 ± 7	NS	0.001	NS
Fat oxidation (% of TEE)	30 ± 7	30 ± 7	31 ± 9	32 ± 10	29 ±8	36 ± 8	0.02	NS	0.03
Nonprotein respiratory quotient	0.891 ± 0.023	0.894 ± 0.023	0.882 ± 0.030	0.882 ± 0.034	0.887 ± 0.030	0.868 ± 0.027	NS	NS	0.05
Carbohydrate oxidation (% of NPEE)	64 ± 8	65 ± 8	61 ± 10	61 ± 12	63 ± 10	57 ± 9	NS	NS	0.05
Fat oxidation (% of NPEE)	36 ± 8	35 ± 8	39 ± 10	39 ± 12	37 ± 10	43 ± 9	NS	NS	0.05

[1] L, lactating; NL, nonlactating; TEE, total energy expenditure; NPEE, nonprotein energy expenditure.
[2] Repeated-measures ANOVA, adjusted for fat-free mass, fat mass, and net energy balance.
[3] $\bar{x}$ ± SD.

work of the heart and lungs. Variation in energy expenditure among subjects was largely due to differences in FFM, which in pregnancy is composed of the expanded plasma, high-energy requiring fetal and uterine tissues, and moderate-energy requiring skeletal muscle mass. In late pregnancy, approximately one-half of the increment in TEE of 1264 kJ/d can be attributed to the fetus. The fetus uses ≈8 mL $O_2 \cdot kg^{-1} \cdot min^{-1}$, or 234 $kJ \cdot kg^{-1} \cdot d^{-1}$. For a 3-kg fetus, this would be equivalent to 703 kJ/d (25). Fat mass, a tissue with low energy requirements, contributed to the variation in energy expenditure, but to a much lesser extent. Our results contrast with those of Bronstein et al (26), who concluded that fat mass, but not FFM, was a significant predictor of BMR and that pregnancy represents a unique condition in which BMR is regulated by fat mass. In our study, FFM was the strongest predictor of TEE, BMR, SMR, and MSMR. It was of interest that serum leptin, which is secreted by fat mass, had an independent effect on energy expenditure, but this effect was not unique to pregnancy.

Room respiration calorimeters have been used to measure the BMR and TEE of pregnant women in only a few studies. Marked variation in the response to pregnancy was seen in 12 British women studied before and throughout pregnancy (3, 27). By 36 wk gestation, the increment in absolute BMR ranged from 8.6% to 35.4%, or −9.2% to 18.6%/kg FFM. Energy-sparing and energy-profligate responses to pregnancy were dependent on prepregnancy body fatness. In 12 Dutch women, the late-pregnancy increment in absolute TEE varied from 9.5% to 26% (28).

In addition to differences in body composition, we identified endocrine and metabolic factors positively associated with rates of energy expenditure. These factors included insulin, IGF-I, fatty acids, leptin, and 24-h urinary excretion of free norepinephrine, epinephrine, and dopamine. Urinary catecholamine excretion allows an integrated assessment of the sympathoadrenal system and a reasonable estimate of plasma concentrations. Our results confirm higher excretion of norepinephrine (29) and dopamine (30) in pregnant women, but are at odds with lower values reported for Gambian women (31). Cortisol was not identified as a significant factor, but elevated concentrations in pregnancy may indirectly exert an effect by promoting the release of and thermogenic response to L-triiodothyronine-mediated norepinephrine and epinephrine (32). Norepinephrine also plays a role in facultative energy expenditure associated with carbohydrate metabolism. Although insulin does not exert a thermogenic effect, it facilitates several energy-requiring processes, including intracellular translocation, oxidation and storage of glucose, lipogenesis, and protein synthesis.

In late gestation, the antiinsulinogenic and lipolytic effects of human chorionic somatomammotropin, prolactin, cortisol, and glucagon contribute to glucose intolerance, insulin resistance, decreased hepatic glycogen, and mobilization of adipose tissue (33). Despite higher serum concentrations of prolactin, cortisol, glucagon, and fatty acids and lower serum glucose concentrations during pregnancy than during the postpartum period, we did not observe a lower respiratory quotient or greater utilization of fatty acids during late pregnancy. On the contrary, we observed higher mean respiratory quotients for 24-h TEE, SMR, MSMR, and BMR during pregnancy than during the postpartum period. Higher basal respiratory quotients were observed during pregnancy by several investigators (4, 7, 12, 13, 34). The respiratory quotient did decline gradually during the overnight fast and the proportion of carbohydrate oxidized became progressively smaller in the postprandial period, but it did so less precipitously during pregnancy than during the postpartum period. These observations are consistent with persistent glucose production in fasting pregnant women, despite lower fasting plasma glucose concentrations. After a 17-h fast, the rates of total glucose production and gluconeogenesis increased, even though the fraction of glucose oxidized and the fractional contribution of gluconeogenesis to glucose production remained unchanged (35, 36). In pregnant women, the sustained energy expenditure and higher respiratory quotient may have reflected the obligatory $\dot{V}O_2$ of the fetus and fetal use of glucose as the primary oxidative substrate. In late gestation, the fetus uses an estimated 17–26 g glucose/d (37), which is well within the increment in carbohydrate oxidation observed in pregnancy.

Energy expenditure during lactation

In lactating women, enhanced efficiency of energy metabolism was not evident at 3 or 6 mo postpartum. On the contrary, higher TEE, SMR, and MSMR values were observed in the L group than in the NL group; differences in BMR were nearly significant (P = 0.06–0.09). Sadurskis et al (8) and Spaaij et al (7) observed a higher RMR (4–5%) in lactating than in nonlactating women. We theorized that the increased energy expenditure represents the energy cost of milk synthesis, because milk energy output was positively correlated with TEE. Higher circulating concentrations of DHEAS and epinephrine may have augmented energy expenditure. Others have not detected a difference in RMR between lactating and nonlactating women (9–11, 15, 38, 39).

In our study, there was a higher mean 24-h respiratory quotient and a higher rate of carbohydrate utilization in the L group than in the NL group at 6 mo postpartum, which is consistent with the preferential use of glucose by the mammary gland. Conflicting results of lower fasting respiratory quotient in lactating compared with nonlactating women (0.82 and 0.85, respectively) (7), as well as no significant differences in respiratory quotient during lactation (10, 15, 39) have been published.

Energy requirements during pregnancy and lactation

Finally, this study has important implications regarding the minimum energy requirements of pregnant and lactating women. The 24-h TEE provides an estimate of energy expenditure under confined conditions. Apart from the 30 min of walking on the treadmill, our subjects were sedentary. Mean ratios of TEE to BMR were between 1.29 and 1.36, which verifies the FAO/WHO/UNU recommendation of 1.4 times the BMR as the minimum energy requirement for maintenance (40). Restricting energy intake to below this minimum, to limit weight gain or control blood glucose, is not advisable in pregnancy. Women who are breast-feeding exclusively need 2000 kJ/d to support milk production, in addition to the minimum energy requirement of 1.4 times the BMR.

In conclusion, increased rates of energy expenditure and carbohydrate utilization were evident during both late pregnancy and lactation. The higher carbohydrate utilization seen at 37 wk gestation was sustained through 6 mo postpartum in lactating women, which is consistent with the preferential use of glucose by the fetus and mammary gland.

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