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The thermic effect of food in normal-weight and overweight pregnant women

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A defective thermic response to food may be an energy-sparing adaptation in both obesity and pregnancy. To evaluate the combined effect of obesity and pregnancy on postprandial thermogenesis, the thermic effect of food was assessed for a 240 min period following a high-carbohydrate meal and a typical mixed meal in nine normal-weight non-pregnant, eight overweight non-pregnant, eight normal-weight pregnant and six overweight pregnant women using indirect calorimetry. A test meal that provided 60% of each subject's measured daily requirement for basal metabolism was used. Pregnant women were studied during weeks 30–35 of gestation. Neither obesity nor pregnancy altered the thermic effect of food, although the response to the mixed meal was greater ($P < 0.01$) than that to the high-carbohydrate meal in all cases. The mean responses for the high-carbohydrate and mixed meals were 26·9 (SD 6·0) and 30·1 (SD 6·2)% baseline energy expenditure respectively, and 7·4 (SD 1·6) and 8·3 (SD 1·6)% of the meal energy load respectively. Obesity and pregnancy were associated with hyperinsulinaemia ($P < 0.005$) following both test meals, suggesting that postprandial thermogenesis was not altered by insulin resistance in this group. The incremental glucose response was elevated ($P < 0.001$) in the pregnant women following both test meals; overweight women tended to have a greater incremental glucose response following the high-carbohydrate meal, but it was not significant ($P = 0.065$). These results do not provide evidence of an impaired thermic response to food in either overweight or third trimester pregnant women.

Thermogenesis: Pregnancy: Obesity

Surveys of dietary intake in pregnant women from developed countries show that energy intakes fall below recommended levels during gestation (Committee on Nutritional Status During Pregnancy and Lactation, Food and Nutrition Board, Institute of Medicine, 1990). This discrepancy between intake and projected energy need has led to the conclusion that energy-sparing metabolic adaptations occur during pregnancy. Recent longitudinal studies of total energy expenditure during pregnancy show that some women may reduce their pregnancy energy requirement by demonstrating a smaller increase in resting metabolism and by reducing activity expenditure (Prentice *et al.* 1989; Goldberg *et al.* 1993). A reduction in energy spent digesting and assimilating food is another mechanism by which the pregnant woman may lower her energy requirement. This third component of total energy expenditure has not been studied extensively in pregnancy. Due to changes in the hormonal milieu and nutrient handling during pregnancy, an altered thermic response to food is feasible.

Research with non-pregnant individuals shows that adjustments in the thermic response to food is one mechanism by which humans regulate energy balance (Garrow, 1986). Furthermore, a defect in the thermogenic response to food has been postulated as a mechanism contributing to the development of obesity. No one has evaluated the combined

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effect of pregnancy and obesity on the thermic response to food. Both these physiological states are characterized by insulin resistance, which has been implicated as a causative factor in lowering the thermic response to food (Puavilai *et al.* 1982; Ravussin *et al.* 1985). If both pregnancy and obesity enhance the efficiency of postprandial metabolism, the energy requirement for overweight pregnant women may differ from that of normal-weight pregnant women. Dietary counselling for overweight pregnant women presents a formidable challenge to optimize fetal growth without encouraging excessive weight gain.

The present study was initiated to determine the effects of pregnancy and obesity on the thermic response to a meal. Thermogenesis was evaluated in four subject groups: normal-weight non-pregnant (NWNP), overweight non-pregnant (OWNP), normal-weight pregnant (NWP) and overweight pregnant (OWP). Pregnant women were evaluated during late gestation because energy needs are greatest at that time. The thermic effect of food (TEF) was assessed following a high-carbohydrate meal and a typical mixed meal. Use of both these meals enabled us to evaluate the hypothesis that insulin resistance is the cause of a defective thermogenic response. If insulin resistance causes a blunted thermogenic response, subject group differences in thermic expenditure would be greatest for the high-carbohydrate meal. Evaluation of a typical breakfast meal also allowed measurement of the response to foods that are representative of those in the usual diet.

SUBJECTS AND METHODS

TEF was assessed in nine NWNP, eight OWNP, eight NWP and six OWP women. Pregnant women were studied during weeks 30–35 of gestation. Overweight was defined as a body mass index (BMI; kg/m^2) $\geqslant 25$ (Garrow, 1981); pregnant women were classified according to their pregravid weight. All women were judged to be in good health, non-smokers, and weight stable (NP women only). Overweight women had a lifelong and family history of obesity and an unsuccessful history of weight loss through energy restriction. The study was approved by the Committees on the Use and Protection of Human Subjects at the University of California, Berkeley and the University of California, San Francisco. Each woman was informed of the study protocol and gave her informed consent. This study was part of a concurrent investigation of basal metabolism and total energy expenditure, further details of which will be reported elsewhere (M. N. Bronstein, R. P. Mak and J. C. King, unpublished results).

Protocol

Before thermogenesis testing, all women were assessed at the San Francisco General Hospital Clinical Research Center (GCRC) for glucose tolerance, health status and for training in energy expenditure measurement. Thermogenesis measurements were scheduled on test days 2 and 3, which were separated by a 2-week period for pregnant women and a 4-week period for non-pregnant women. Non-pregnant women were studied during the follicular phase of their menstrual cycle. Because prior dietary intake may modify the thermic response to food, subjects consumed a constant diet at home for 4 d before the test days. The constant diet provided 14% energy from protein, 31% from fat, and 55% from carbohydrate. The energy content of the diet was varied to provide 1·38 × BMR, which was the average total energy expenditure of a group of sedentary British women (Prentice *et al.* 1985). All the pregnant women were given a minimum of 9·20 MJ/d (2200 kcal/d).

Subjects were admitted to the GCRC the night before both test days. At 06.30 hours the next morning, BMR was measured by open circuit, indirect calorimetry using the Douglas bag technique. The BMR measurement served as the baseline energy expenditure value for the determination of the TEF. After measurement of BMR, an indwelling catheter was

inserted in an arm vein for blood sampling. Cannula patency was maintained by means of a constant saline drip. At 30 min after insertion of the catheter, subjects received one of the two test meals; the meals were consumed in 20–25 min. Breath gas collection commenced 5 min after completion of the meal. A total of sixteen 10 min Douglas bags were collected over a 240 min period; 5 min breaks were allowed between each bag. For each 10 min measurement period, 2 min were allowed for adaptation to the apparatus and 8 min for breath gas collection. Subjects were in a reclining position (45° angle) during the thermogenesis measurement, and were told to lie quietly, but were allowed to read, listen to the radio, or watch television. A bathroom break was given to all subjects at 120 min, additional bathroom trips were allowed if necessary. All measurements were performed in a thermoneutral environment. Blood samples were drawn for hormone and metabolite analysis before the test meals and at 30 min, 1 h, 2 h, 3 h and 4 h postprandially.

Test meals

Two test meals, a high-carbohydrate meal and a mixed meal, were evaluated in a random order. The energy content of both test meals equalled 60% of the subject's measured daily BMR level. The high-carbohydrate meal consisted of Polycose (Ross Laboratories, Columbus, OH, USA), orange juice, wholemeal toast, butter and jam. The energy distribution was 5% protein, 10% fat and 85% carbohydrate. The mixed meal comprised orange juice, low-fat milk, scrambled eggs, wholemeal toast, butter and grape jam. The energy distribution was 15% protein, 35% fat and 50% carbohydrate.

Initially, a high-carbohydrate meal that consisted of orange sherbet (sorbet), canned pears in syrup and fresh banana was used for five of the subjects (two NWNP, two NWP, one OWP). The energy distribution of this meal was 3% protein, 4% fat and 93% carbohydrate. Due to a complaint by one of the subjects of slight nausea, this meal was discontinued in favour of the Polycose meal. The two high-carbohydrate meals differed slightly in composition. For a 3·8 MJ meal the sherbet/fruit meal provided 103·6 g sucrose, 48·5 g glucose, 34·3 g fructose and 23·6 g complex carbohydrate whereas the Polycose meal provided 21·4 g sucrose, 9·0 g glucose, 112·5 g glucose polymer, 69 g fructose and 44·6 g complex carbohydrate. Although the components of the two high-carbohydrate meals differed, the energy expenditure and respiratory quotient data from both have been included in the analysis of the TEF, as both high-carbohydrate meals served as good comparisons to the mixed meal and enabled us to address the question of whether a blunted thermogenic response was due to insulin resistance. Analysis of the data, excluding these five subjects is also presented.

Energy expenditure measurements and calculations

Indirect calorimetry measurements and the calculation of energy expenditure were performed using the equation of Weir (1949). Urine collections (24 h) were obtained on the day before each test day and analysed for total N using a micro-Kjeldahl method (Block & Weiss, 1956). Non-protein respiratory quotient (NPRQ) and the fraction of non-protein O_2 consumption due to carbohydrate and lipid were computed (Vernet *et al.* 1986). The average postprandial NPRQ and substrate utilization were computed for the sixteen postprandial time points.

To compute total energy expenditure for the 240 min postprandial period the formula for the area of a trapezoid was used. The cost of BMR during the test was estimated from the morning BMR measurement and extrapolated for the 240 min period. TEF was computed from the arithmetic difference between total energy expended for the 240 min period and BMR. The TEF (kJ) was expressed relative to test meal size (TEF/test meal size (kJ) × 100) and the cost of BMR ((TEF/BMR) × 100).

Oral glucose tolerance test (OGTT)

Glucose tolerance was evaluated on test day 1; pregnant women were scheduled for study at 28–30 weeks gestation. Following a fasting (10 h) blood sample, subjects consumed 100 g glucose in the form of a non-caffeinated, 'cola-like' (Lancer, St Louis, MO, USA) beverage. Blood samples were drawn at 1, 2 and 3 h time points for glucose analysis by the clinical laboratory at the San Francisco General Hospital. Pregnant women were not accepted for study if two or more plasma glucose values met or exceeded the following levels: fasting, 5·72 mmol/l; 1 h, 10·44 mmol/l; 2 h, 9·16 mmol/l; and 3 h, 7·94 mmol/l (O'Sullivan & Mahan, 1964). Non-pregnant women were not accepted for study if any plasma glucose values met or exceeded the following levels: fasting, 6·38 mmol/l; 1 h, 11·10 mmol/l; 2 h, 7·77 mmol/l; and 3 h, 7·77 mmol/l (National Diabetes Data Group, 1979).

Insulin and glucose analysis

Insulin and glucose concentrations were measured in all blood samples from the OGTT. Serum immunoreactive insulin was analysed by a single-antibody, solid-phase, radioimmunoassay (Insulin RIA kit, Diagnostic Products Corp., Los Angeles, CA, USA). Plasma glucose was analysed by an oxidase–peroxidase enzymic kit (Sigma Diagnostics, Sigma Chemical Co., St. Louis, MO, USA). All analyses were performed in duplicate; if the coefficient of variation was greater than 5%, the analysis was repeated. The integrated areas under the insulin and glucose curves were computed using the formula for the area of a trapezoid.

Statistical analysis

Results were analysed using Statistical Analysis Software (SAS Institute Inc., 1985). A series of one-way analyses of variance (ANOVA) was performed to compare the four subject groups with respect to age, anthropometric characteristics, glucose tolerance, BMR and pregnancy outcome. Two-way ANOVA were performed to determine the effect of excess body weight and pregnancy on the preprandial level of insulin and glucose, along with the incremental responses of insulin and glucose following the two meal challenges. A series of three-factor repeated measures ANOVA with two grouping factors and one trial factor was performed. Body weight and pregnancy were the grouping factors. Time was the trial factor for the analysis of the time course of energy expenditure following the test meal challenges. Test meal was the trial factor for the analysis of the TEF and preprandial and postprandial NPRQ. A three-factor repeated measures ANOVA, with body weight and pregnancy as the grouping factors and time as the trial factor, was also utilized to evaluate preprandial and postprandial insulin and glucose values. For the latter analysis the insulin and glucose data were log-transformed due to the observation of large and unequal variances between subject groups. Log transformation of the data also enabled us to look at the percentage changes in plasma insulin and glucose levels from baseline. For all two way ANOVA and three-factor repeated measures ANOVA, if there were no interactions, the P values associated with the main effects (i.e. weight, pregnancy, trial factor) were used to assess statistical significance. If there were significant results, ANOVA was compared to the cell means, using Tukey's Studentized Range test. For all statistical analyses the level of significance was $P < 0{\cdot}05$. All values are reported as means and standard deviations (SD), except where otherwise noted.

RESULTS

All subjects were Caucasian except for two non-pregnant subjects who were black (Table 1). As expected, overweight women differed significantly ($P < 0{\cdot}05$) from the normal-weight women with respect to percentage body fat as determined by both skinfolds and

Table 1. *Subject profile*

	Non-pregnant				Pregnant			
	NW (*n* 9)		OW (*n* 8)		NW (*n* 8)		OW (*n* 6)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (years)	28·2[a]	3·7	30·8[a]	3·5	27·2[a]	2·8	27·3[a]	3·4
Current pregravid wt (kg)*	60·3	6·4	100·2	22·6	59·6	4·2	87·6	16·7
Height (m)	1·662[a]	0·079	1·634[a]	0·049	1·688[a]	0·039	1·656[a]	0·047
BMI (kg/m²)†	21·8	1·3	37·4	7·7	20·9	1·0	31·8	4·9
% Body fat-SF‡	27·8[a]	4·7	43·0[b]	3·3	31·5[a]	6·2	43·1[b]	4·1
% Body fat-D§	24·7[a]	5·3	46·4[c]	1·8	34·0[b]	2·6	46·5[c]	3·7
Fasting glucose (mmol/l)	4·5[b]	0·4	4·5[b]	0·4	3·9[a]	0·4	4·3[ab]	0·2
Glucose area (mmol/l.h)‖	1·9[a]	2·2	3·6[a]	1·4	8·2[b]	2·3	7·0[b]	0·4
Basal metabolic rate (MJ/d)	5·34[a]	0·43	6·57[b]	1·16	6·61[b]	0·62	8·34[c]	0·85

NW, normal weight; OW, overweight.
[a, b, c] Mean values within a row not sharing a common superscript letter were significantly different, $P < 0·05$.
* Weight reported by pregnant women.
† As determined from pregravid weight for the pregnant women.
‡ % Body fat at time of study, calculated from skinfolds.
§ % Body fat at time of study calculated from densitometry.
‖ Integrated over 3 h after an oral 100 g glucose load.

densitometry. Age and height were similar in all subject groups. Fasting glucose was lower ($P < 0·05$) in the NWP group compared with the two non-pregnant groups. All women were judged to be glucose tolerant. The integrated glucose response to the 100 g oral glucose load was significantly greater ($P = 0·001$) for pregnant women. There was no effect of excess body weight ($P = 0·86$) on the clearance of glucose following the 100 g glucose challenge. BMR was increased ($P < 0·001$) by both excess body weight and pregnancy (Table 1). The measurement of BMR before both days of thermogenesis testing was highly reproducible; the correlation coefficient for duplicate measurements was 0·97 ($P < 0·001$).

All women had a full-term pregnancy (> 37 weeks). Gestational weight gain did not differ between normal-weight and overweight women (17·4 (SD 7·0) *v.* 14·0 (SD 4·9) kg; $P = 0·14$). Overweight women had significantly ($P < 0·05$) heavier (4·04 (SD 0·40) *v.* 3·33 (SD 0·33) kg) and longer (554 (SD 25) *v.* 508 (SD 10) mm) infants than normal-weight women.

Fig. 1 portrays the total energy expenditure following both test meals. For the high-carbohydrate meal there were no group differences in the energy response; energy expenditure rose significantly following the test meal and failed to decline significantly by the end of the test period. As there was no group-by-time interaction, both excess body weight and pregnancy increased energy expenditure at all time points. For the mixed meal the responses of the normal-weight and overweight women differed. The overweight women had a significant transient increase in energy expenditure above the initial rise at the end of 120 min; this transient rise was not seen in the normal-weight women. The complete thermogenic response was not measured, as expenditure failed to return to baseline or drop significantly by the end of the test for either meal and for all subject groups.

The thermogenic response data are summarized in Table 2 and Fig. 2. As test meal size was based on measured BMR (i.e. 0·60 × 24 h BMR), the test meal size was increased by both excess body weight ($P < 0·001$) and pregnancy ($P = 0·001$). The TEF (kJ) was higher among overweight women ($P = 0·024$) than normal-weight women, but was not

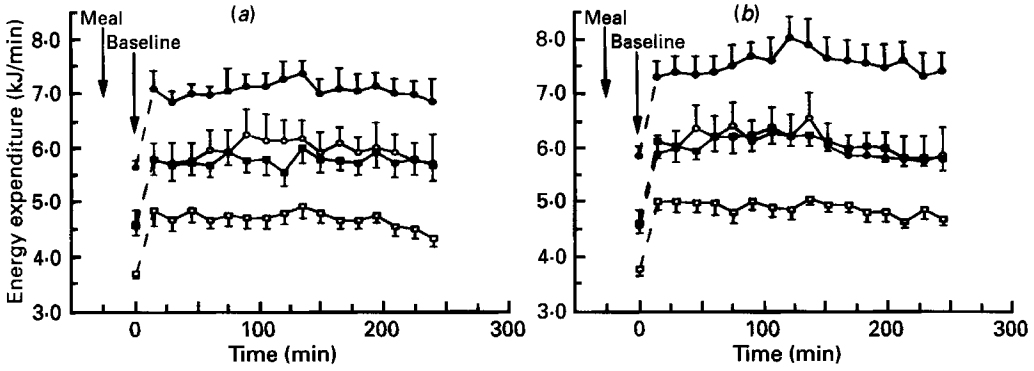

Fig. 1. Total energy expenditure by normal-weight and overweight pregnant and non-pregnant women following consumption of (*a*) a high-carbohydrate meal or (*b*) a mixed meal. Meals were consumed 25–30 min before initiation of energy expenditure measurements. The baseline measurement was performed before consumption of the meal. (□), Normal-weight, non-pregnant (*n* 9); (○), overweight, non-pregnant (*n* 8); (■), normal-weight pregnant (*n* 8); (●), overweight, pregnant (*n* 6). Values are means with their standard errors indicated by vertical bars. For details of meals and procedures, see pp. 262–264.

Table 2. *Thermogenic responses to high-carbohydrate and mixed meals by normal weight (NW) and overweight (OW) pregnant and non-pregnant women**

(Mean values and standard deviations)

	Non-pregnant				Pregnant				
	NW (*n* 9)		OW (*n* 8)		NW (*n* 8)		OW (*n* 6)		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Significance†
Energy value of test meal (MJ)	3·46	0·14	3·96	0·62	3·90	0·45	4·69	0·38	Weight ($P < 0·001$)
Range	(3·33–3·77)		(3·22–5·21)		(3·35–4·48)		(4·35–5·44)		Pregnancy ($P = 0·001$)
Energy expenditure (kJ) for TEF									
Carbohydrate	243	61	320	85	283	54	338	109	Weight ($P = 0·02$)
Mixed	269	30	352	90	336	75	374	132	Pregnancy ($P = 0·17$)
									Meal ($P < 0·01$)
TEF (% increase relative to BMR)									
Carbohydrate	27·4	6·6	29·0	5·6	25·9	4·0	24·7	8·0	Weight ($P = 0·97$)
Mixed	29·8	1·8	32·3	6·5	30·4	6·8	27·3	9·2	Pregnancy ($P = 0·18$)
									Meal ($P < 0·01$)
TEF (% metabolizable energy load)									
Carbohydrate	7·0	1·7	8·0	1·4	7·2	0·9	7·2	2·3	Weight ($P = 0·49$)
Mixed	7·8	0·7	8·8	1·7	8·6	1·3	7·9	2·7	Pregnancy ($P = 0·74$)
									Meal ($P < 0·01$)

TEF, thermic effect of food.

* For details of meals and procedures, see pp. 262–264.

† Three-factor repeated measures ANOVA was used. The significance of two grouping factors (weight, pregnancy) and the one trial factor (test meal) is given.

affected by pregnancy ($P = 0·17$). There was no significant effect of either excess body weight or pregnancy when TEF was expressed as a function of either BMR or energy load of the meal. The response to the mixed meal was consistently greater than that to the high-carbohydrate meal ($P < 0·01$). The average TEF values, as a percentage of the BMR, were

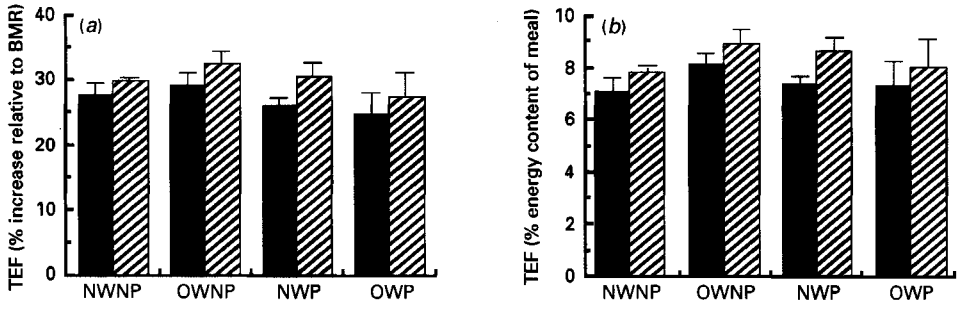

Fig. 2. The thermic effect of food (TEF) in normal-weight and overweight, pregnant and non-pregnant women, expressed as (*a*) the percentage increase in expenditure relative to baseline expenditure and (*b*) a percentage of the metabolizable energy content of the meal ingested, following consumption of a high-carbohydrate meal (■) and a mixed meal (▨). NWNP, normal-weight, non-pregnant (*n* 9); OWNP, overweight non-pregnant (*n* 8); NWP, normal-weight pregnant (*n* 8); OWP, overweight pregnant (*n* 6). Values are means with their standard errors indicated by vertical bars. Neither excess body weight nor pregnancy was associated with an altered TEF; the response to the mixed meal was greater ($P < 0{\cdot}01$) than that to the high-carbohydrate meal. For details of meals and procedures, see pp. 262–264.

Table 3. *Preprandial and average postprandial non-protein respiratory quotient (NPRQ) values for high-carbohydrate and mixed meals consumed by normal weight (NW) and overweight (OW) pregnant and non-pregnant women**

(Mean values and standard deviations)

	Non-pregnant				Pregnant				
	NW (*n* 9)		OW (*n* 8)		NW (*n* 8)		OW (*n* 6)		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Significance†
Preprandial NPRQ									
Carbohydrate	0·80	0·08	0·77	0·04	0·83	0·05	0·81	0·03	Weight ($P = 0{\cdot}80$)
Mixed	0·75	0·06	0·79	0·05	0·80	0·04	0·81	0·04	Pregnancy ($P = 0{\cdot}02$)
									Meal‡
Average postprandial NPRQ									
Carbohydrate	0·95	0·04	0·94	0·04	0·93	0·05	0·92	0·02	Weight ($P = 0{\cdot}97$)
Mixed	0·86	0·08	0·86	0·06	0·86	0·03	0·88	0·03	Pregnancy ($P = 0{\cdot}64$)
									Meal ($P < 0{\cdot}001$)

* For details of meals and procedures, see pp. 262–264.

† Three-factor repeated measures ANOVA was employed: significance of two grouping factors (Weight; Pregnancy) and the one trial factor (test meal) are given.

‡ Weight group × test meal interaction was significant ($P = 0{\cdot}04$). The two fasting measurements made for the normal weight women differed significantly.

26·9 (SD 6·0) and 30·1 (SD 6·2) % for the high-carbohydrate meal and the mixed meal respectively; the average response, expressed as a percentage of the meal load, was 7·4 (SD 1·6) for the high-carbohydrate meal and 8·3 (SD 1·6) % for the mixed meal. For the five subjects who received the sherbet/fruit high-carbohydrate meal, the TEF values expressed as a percentage of the meal energy load were 6·1 (NWNP), 5·5 (NWNP), 7·4 (NWP), 7·0 (NWP) and 5·3 (OWP) %. The TEF results presented were identical with or without inclusion of the data obtained from these five subjects.

Preprandial NPRQ were obtained for all subjects (Table 3). The pregnant women had a higher ($P = 0{\cdot}02$) preprandial NPRQ than the non-pregnant women, indicating that

Table 4. *Insulin (μU/ml) and glucose (mmol/l) levels before and following the consumption of a high-carbohydrate meal by normal weight (NW) and overweight (OW) pregnant and non-pregnant women**

(Mean values and standard deviations)

	Non-pregnant				Pregnant			
	NW (*n* 7)		OW (*n* 8)		NW (*n* 6)		OW (*n* 5)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Insulin (μU/ml)†								
Preprandial	5·3[a]	1·3	12·0[a]	7·3	6·6[a]	3·2	12·2[a]	3·0
30 min	117·3[d]	48·7	149·6[c]	71·4	166·0[c]	92·9	234·0[b]	123·4
1 h	75·4[cd]	45·1	144·5[c]	83·8	151·8[c]	65·0	305·0[b]	131·8
2 h	68·8[cd]	40·6	135·1[c]	65·7	140·9[c]	74·9	320·0[b]	218·6
3 h	46·5[bc]	21·1	107·7[bc]	70·3	124·8[bc]	82·1	232·0[b]	53·8
4 h	27·7[b]	12·4	61·5[b]	45·7	60·2[b]	45·7	146·0[b]	48·0
Glucose (mmol/l)†								
Preprandial	4·37[a]	0·53	4·40[a]	0·68	3·58[a]	0·87	3·81[a]	0·54
30 min	6·57[b]	1·37	7·22[b]	2·01	6·82[b]	1·87	8·64[c]	1·42
1 h	5·30[ab]	1·19	6·72[b]	1·60	7·02[b]	2·47	9·26[c]	1·22
2 h	5·21[ab]	1·03	5·53[ab]	1·21	6·45[b]	1·66	7·45[bc]	1·54
3 h	4·71[ab]	0·71	5·58[ab]	1·14	6·12[b]	2·64	6·82[bc]	0·88
4 h	4·69[ab]	0·94	4·92[a]	1·35	5·19[b]	1·42	6·15[b]	1·53

[a, b, c, d] Mean values within a column with unlike superscript letters were significantly different, $P < 0·05$.

* For details of meals and procedures, see pp. 262–264. Values are for subjects consuming the 'Polycose' high-carbohydrate meal only. Comparisons are made within each of the four groups only. Due to significant interaction of pregnancy and weight groups with time, the effect of pregnancy and weight group could not be directly assessed.

† Statistical analyses were performed on log transformed data for both insulin and glucose.

carbohydrate represented a higher proportion of fasting fuel for the pregnant women. Excess body weight ($P = 0·80$) did not affect the preprandial NPRQ. There was a significant body weight × test meal interaction ($P = 0·04$). The preprandial NPRQ of the normal-weight women was lower than that of the overweight before the mixed meal. Using the mean of the two preprandial NPRQ measurements, the calculated interindividual variability was 9·1% for the NWNP, 5·8% for the OWNP, 5·5% for the NWP and 4·3% for the OWP groups. The postprandial NPRQ values following both the high-carbohydrate meal and the mixed meal were not affected by either weight ($P = 0·97$) or gestational status ($P = 0·64$). The meal effect was significant ($P < 0·001$), however; as expected, the mean postprandial NPRQ following the mixed meal was lower. Exclusion of the five subjects who received the sherbet/fruit high-carbohydrate meal did not alter the postprandial NPRQ findings.

Insulin and glucose levels before and following the high-carbohydrate meal are presented only for the twenty-six subjects who received the Polycose high-carbohydrate meal (Table 4). Preprandially, insulin was elevated among the overweight women ($P = 0·002$) but was not modified by pregnancy ($P = 0·69$). Baseline glucose values were lower among the pregnant women ($P = 0·017$), but were not altered by excess body weight ($P = 0·66$). Postprandially, both excess body weight ($P = 0·003$) and pregnancy ($P = 0·001$) were associated with higher serum insulin levels. Postprandial plasma glucose levels of pregnant women were higher ($P = 0·032$) than those of non-pregnant women; overweight women tended to have higher plasma glucose levels postprandially, but the difference was not significant ($P = 0·072$). Due to the significant interaction of pregnancy and weight groups

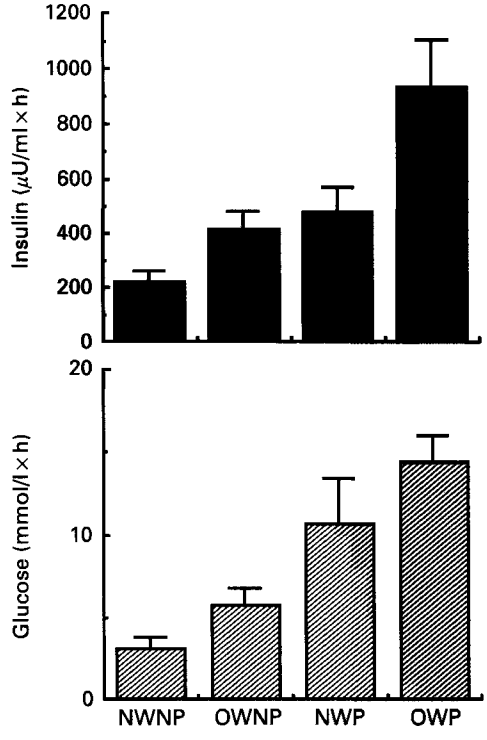

Fig. 3. Incremental insulin and glucose responses in normal-weight and overweight, pregnant and non-pregnant women following consumption of a high-carbohydrate meal. Values are for women consuming the 'Polycose' high-carbohydrate meal only. NWNP, normal-weight, non-pregnant (n 7); OWNP, overweight non-pregnant (n 8); NWP, normal-weight, pregnant (n 6); OWP, overweight pregnant (n 5). Values are means with their standard errors indicated by vertical bars. The incremental insulin response was significantly increased by both excess body weight ($P = 0{\cdot}005$) and pregnancy ($P = 0{\cdot}001$). The incremental glucose response was only greater ($P < 0{\cdot}001$) among pregnant women; the effect of obesity ($P = 0{\cdot}065$) was not significant. For details of meals and procedures, see pp. 262–264.

with time, each of the four subject groups was evaluated separately with respect to the time course of postprandial insulin and glucose levels. Log-transformed plasma insulin levels showed a significant rise and decline in all subject groups, except for the OWP group. In this group insulin levels failed to decline significantly after the initial rise. Log-transformed plasma glucose level rose significantly in all subject groups. In both non-pregnant groups glucose levels had returned to a level not significantly different from baseline by 2 h. In both pregnant groups glucose levels had not returned to baseline by the end of the 4 h study. The incremental insulin and glucose responses over baseline following the Polycose high-carbohydrate meal are shown in Fig. 3. The incremental insulin response was significantly greater among both overweight ($P = 0{\cdot}005$) and pregnant ($P = 0{\cdot}001$) women. The incremental glucose response was significantly greater in the pregnant women ($P < 0{\cdot}001$), but not in the overweight women ($P = 0{\cdot}065$).

Preprandial insulin and glucose levels on the day of the mixed meal did not differ from those measured on the day of the high-carbohydrate meal (Table 5). The postprandial insulin level was significantly higher among overweight ($P = 0{\cdot}002$) and pregnant ($P = 0{\cdot}001$) women. Postprandial glucose concentrations were not affected by either excess body weight ($P = 0{\cdot}15$) or pregnancy ($P = 0{\cdot}35$) following the mixed meal. Due to the significant interaction of pregnancy and weight groups with time, each of the four subject

Table 5. *Insulin (μU/ml) and glucose (mmol/l) levels before and following the consumption of a mixed meal by normal weight (NW) and overweight (OW) pregnant and non-pregnant women**

(Mean values and standard deviations)

	Non-pregnant				Pregnant			
	NW (*n* 9)		OW (*n* 7)		NW (*n* 8)		OW (*n* 5)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Insulin (μU/ml)†								
Preprandial	5·1[a]	1·3	12·8[a]	8·4	7·5[a]	1·7	16·0[a]	10·9
30 min	61·1[e]	24·2	126·8[d]	77·9	151·5[d]	81·1	245·6[d]	47·8
1 h	42·9[de]	23·2	113·6[d]	69·7	122·1[d]	88·6	161·4[cd]	72·4
2 h	29·0[cd]	7·0	79·4[cd]	64·1	88·4[d]	57·4	117·6[bcd]	31·0
3 h	21·2[c]	4·9	46·8[bc]	29·7	36·8[c]	15·7	105·6[bc]	70·4
4 h	12·0[b]	5·7	29·7[b]	20·9	18·2[b]	11·6	65·6[b]	34·1
Glucose (mmol/l)†								
Preprandial	4·71[a]	0·67	4·62[a]	0·59	3·62[a]	0·73	4·35[a]	0·72
30 min	5·92[b]	1·41	5·73[a]	1·02	6·62[d]	1·52	7·35[b]	2·00
1 h	4·29[a]	0·61	5·10[a]	1·33	5·78[cd]	0·73	6·59[b]	1·54
2 h	4·66[ab]	1·16	5·53[a]	0·86	5·50[cd]	1·37	5·58[ab]	0·83
3 h	5·05[ab]	0·88	5·19[a]	0·72	4·70[bc]	1·45	5·30[ab]	1·30
4 h	5·07[ab]	0·80	4·99[a]	0·50	3·88[b]	1·18	5·25[ab]	0·71

[a, b, c, d] Mean values within a column with unlike superscript letters were significantly different, $P < 0·05$.

* For details of meals and procedures, see pp. 262–264. Comparisons are made within each of the four groups only. Due to significant interaction of pregnancy and weight groups with time the effect of pregnancy and weight group could not be directly assessed.

† Statistical analyses were performed on log transformed data for both insulin and glucose.

groups was evaluated separately with respect to the time course of postprandial insulin and glucose levels. Log-transformed plasma insulin levels showed a significant rise and decline in all subject groups. Log-transformed plasma glucose rose significantly only in the pregnant groups. In the NWP women glucose levels had not returned to baseline by 4 h. In the OWP women glucose levels had returned to baseline by 2 h. The incremental insulin response to the mixed meal was increased by excess body weight ($P = 0·005$) and pregnancy ($P = 0·001$) (Fig. 4); the incremental glucose response was greater ($P < 0·001$) in the pregnant women, but was not affected by body-weight status ($P = 0·36$).

DISCUSSION

The TEF is composed of obligative and facultative components (Trayhurn & James, 1981; Acheson *et al.* 1984). Obligative costs are those incurred by the energy demands for digestion, absorption and storage of nutrients. Facultative expenditure is energy spent in excess of that required for the processing of nutrients. Obesity has been linked with a reduction in both obligative and facultative expenditure (Astrup *et al.* 1990; Segal *et al.* 1992*a*). Decreased obligative costs in the overweight individual are associated with insulin resistance and altered glucose handling (Ravussin *et al.* 1985), whereas differences in facultative expenditure are associated with stimulation of the sympathetic nervous system, Na pumping, substrate recycling and protein synthesis (Newsholme, 1980). We proposed that pregnancy induces changes in obligative and facultative expenditure. An increased rate of synthesis of new tissue due to fetal and maternal growth could increase obligative

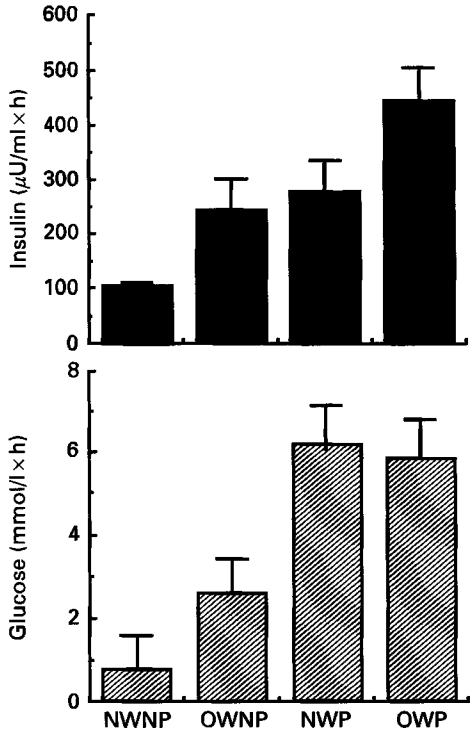

Fig. 4. Incremental insulin and glucose responses in normal-weight and overweight, pregnant and non-pregnant women following consumption of a mixed meal. NWNP, normal-weight, non-pregnant (n 9); OWNP, overweight non-pregnant (n 7); NWP, normal-weight pregnant (n 8); OWP, overweight pregnant (n 5). Values are means with their standard errors indicated by vertical bars. The incremental insulin response was significantly increased by both excess body weight ($P = 0{\cdot}005$) and pregnancy ($P = 0{\cdot}001$). The incremental glucose response was only greater ($P < 0{\cdot}001$) among pregnant women; the effect of obesity ($P = 0{\cdot}356$) was not significant. For details of meals and procedures, see pp. 262–264.

expenditure. Alternatively, hormonal changes may enable the pregnant woman to reduce thermogenesis expenditure and offset, at least in part, the increased energy requirement for basal metabolism and tissue deposition. For example, insulin resistance, which accompanies pregnancy, could reduce postprandial expenditure.

There was no evidence in the present study, however, that the TEF to either a high-carbohydrate meal or a mixed meal was modified by pregnancy or obesity. Both obesity and pregnancy are characterized by a reduction in insulin sensitivity, and insulin resistance has been associated with a reduced rate of non-oxidative glucose disposal (i.e. storage), which has a higher thermogenic response than glucose oxidation (Theibaud *et al.* 1983; Ravussin *et al.* 1985). Both obesity and pregnancy were associated with a hyperinsulinaemic response following both meal challenges in the present study, with the response being about two-fold greater following the high-carbohydrate meal. However, unlike the findings of some researchers (Golay *et al.* 1982; Robinson *et al.* 1993), there was no evidence that postprandial expenditure and insulin response were related. Others have also failed to see an impaired thermogenic response to either glucose (Welle & Campbell, 1983) or a high-carbohydrate meal (Schwartz *et al.* 1985) in glucose-tolerant obese women who were hyperinsulinaemic. Variability in the glucose tolerance of the subjects may explain why results differ among studies. Segal *et al.* (1990*b*, 1992*b*) found thermogenesis to be more

closely related to postprandial glucose levels than to insulin levels. All the subjects in our study were glucose tolerant. Furthermore, the incremental glucose response was not elevated following either meal in the obese women, but it was significantly elevated in the pregnant group.

The thermogenic response to a mixed meal was greater than the thermic response to a high-carbohydrate meal in all groups. Because several studies have reported that protein is a greater stimulus to thermogenesis than is carbohydrate (Nair *et al.* 1983; Zed & James, 1986; Steiniger *et al.* 1987), we believe that the most likely explanation for the greater response to the mixed meal was the increased protein content. In contrast, fat has been shown to induce a lower (Schwartz *et al.* 1985; Lean & James, 1988) or similar (Abbott *et al.* 1990; Kinabo & Durnin, 1990) thermic response to that induced by carbohydrate.

Studies of the effect of pregnancy on thermogenesis have been inconsistent. Nagy & King (1984) failed to find a reduction in the TEF in early and late pregnancy following a 3·14 MJ (750 kcal) mixed meal challenge. Prentice *et al.* (1989) similarly noted that there was little variability in thermogenesis in eight women studied longitudinally over the course of pregnancy. Illingworth *et al.* (1987), however, found a reduction in postprandial expenditure in the second trimester (25–28 weeks gestation) of pregnancy, but not during early or late gestation. The energy saving during mid-gestation was small and amounted to a difference of only 22 kJ (5 kcal), or 1% of the energy load consumed. Robinson *et al.* (1993) observed 29 kJ (7 kcal) and 55 kJ (13 kcal) savings in postprandial expenditure in the second and third trimesters of pregnancy respectively. In that study postprandial thermogenesis correlated positively with insulin sensitivity, as assessed by the decline in plasma glucose following a bolus of intravenous insulin. The authors concluded that insulin insensitivity was responsible for the reduction in thermogenesis. They estimated that 38·6 MJ, or about 13% of the total energy requirement, was saved by the fall in thermogenesis during the later two trimesters. It is difficult to determine why the results of these studies differ. All pregnant women studied have been glucose tolerant despite differences in insulin sensitivity. It seems most likely that differences in study design and experimental methodology, along with the heterogeneity amongst pregnant women, explain the different results. Since study design and characteristics of the subject population may explain specific differences in the thermogenic response, specific features of the present study are discussed further.

We measured thermogenesis for a 240 min period. We failed, however, to measure the complete thermogenic response because energy expenditure did not return to baseline by the end of the period. Differences might have been detected if we had measured the complete response. Others have shown, however, that differences can be detected with a shorter measurement period (Pittet *et al.* 1976; Schutz *et al.* 1984*b*; Segal *et al.* 1990*b*). Segal and co-workers (1990*b*) found that a 3 h period was just as effective as a 6 h measurement period.

We based the size of the meal challenge on the BMR. This resulted in the pregnant and overweight women receiving a significantly larger energy load. A meal challenge of variable size has been advocated on the rationale that differences in metabolic body mass should be taken into account when assessing the TEF (Bessard *et al.* 1983). Segal *et al.* (1990*a*) found similar differences in thermogenesis between lean and obese men, however, regardless of whether a constant or a relative meal challenge was utilized.

To optimize our ability to detect a difference in thermogenesis we standardized our subject population for criteria known to affect TEF. Women selected were non-diabetic, weight stable, and of a similar age. Additionally, prior dietary intake was standardized for the 4 d before thermogenesis testing. Overweight women were further selected for a family history of obesity and a personal history of difficulty in weight reduction. With all these

efforts to control for confounding variables, interindividual variability was great in all subject groups and for both test meals; variability was greatest in the OWP group. Others have noted that TEF is particularly variable among overweight individuals (Schutz *et al.* 1984*a*). Thus, although a defect in thermogenesis may represent an energy-sparing adaptation in some overweight and pregnant individuals, it does not appear to be a defined characteristic for either of these physiological states.

The reproducibility of thermogenesis measurements within a given individual is another issue of concern. While Segal *et al.* (1992*b*) found intra-individual variability to be minimal, others have reported poor intra-individual reproducibility, with coefficients of variation averaging from about 15 to 30% for duplicate measurements (Den Besten *et al.* 1988; Westrate *et al.* 1990; Bukkens *et al.* 1991; Miles *et al.* 1993). If the within-subject variation is this great, the number of observations needed to detect differences in postprandial expenditure exceeds the usual sample sizes. For example, Miles *et al.* (1993) calculated that sixty observations would be needed to detect a difference of 42 kJ (10 kcal) in the TEF if the within-subject coefficient of variation was 26·4% for triplicate measurements in six subjects. The reproducibility of basal metabolic expenditure was very good in the present study (coefficient of variation was 2%); intra-individual reproducibility was not measured, however. It is possible that poor intra-individual reproducibility may have hindered our ability to detect subject group differences.

It has been proposed that individuals who tend to be in positive energy balance, such as the chronically obese, have a defect in their ability to adjust lipid oxidation to intake (Tremblay, 1992). If these individuals consume a high-fat diet, an imbalance occurs with the end result being an increase in lipid stores. This diminished capacity to oxidize lipid is thought to be the result of insulin resistance. There was no evidence of a reduced capacity to oxidize lipid in our overweight women, based on pre- and postprandial measurements of NPRQ. Lipid oxidation was reduced in the pregnant women compared with the non-pregnant women, however. Several others have also reported a higher fasting RQ, or a lower rate of lipid oxidation, in pregnant women (Denne *et al.* 1991; Robinson *et al.* 1993). In contrast, lipid utilization is increased during the latter half of gestation in experimental animals (Knopp *et al.* 1970, 1973). It is also reported that the lipolytic activity of adipocytes isolated from third trimester pregnant women is elevated (Elliot, 1975). If lipid oxidation is blunted during gestation, a pregnant women consuming a high-fat diet may store fat more readily than a non-pregnant woman. Thus, while there may be no substantial defect in thermogenesis during pregnancy, subtle differences in the routeing of nutrients may explain why pregnant women are more predisposed to being in positive energy balance.

In summary, the combination of obesity and late gestation did not result in a reduction in the TEF, despite hyperinsulinaemia and some impairment in glucose clearance. Thermogenesis may be blunted at other points in gestation and perhaps in pregnant women with limited access to food. Alternatively, our sample size may not have been large enough to detect small differences in the TEF between subject groups.

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