Thermic response to isoenergetic protein, carbohydrate or fat meals in lean and obese subjects

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Summary
1. The thermic response of five lean and five obese subjects was measured by indirect calorimetry before, and for 157.5 min after a meal of protein, carbohydrate or fat, each of which provided 1.25 MJ. The change in plasma glucose, insulin and (in the case of the carbohydrate meal) the rate of exogenous glucose oxidation was also measured.

2. There was no significant difference between the lean and obese groups in the magnitude of the thermic response to any of the three meals. In both weight groups the response was largest and most prolonged after the protein meal ($P < 0.01$).

3. The obese group showed a higher concentration of fasting plasma insulin ($P < 0.01$) and a larger increase in plasma glucose ($P < 0.05$) after the carbohydrate meal, but there was no significant difference in the oxidation of exogenous glucose when compared with the lean group.

4. Previous studies on dietary-induced thermogenesis in lean and obese subjects have given conflicting results. In general reports of decreased thermogenesis in obese subjects are characterized by either (a) high pre-meal metabolic rates in the obese group, especially in diabetic subjects, or (b) a group classified as 'normal' who have been selected for their high thermogenic capacity.

Key words: diet, glucose oxidation, glucose tolerance, obesity, thermogenesis.

Introduction
The connection between obesity and glucose intolerance is well established [1]. When normal volunteers are made obese by experimental overfeeding their glucose tolerance decreases despite an increased plasma insulin concentration [2], and among the children of diabetic parents those most obese are most likely to become diabetic [3]. It has also been reported that obese women show a smaller increase than lean women in resting metabolic rate ('thermic response') after an oral load of 50 g of glucose [4], and that the glucose intolerance of obesity is in part explained by a decrease in the rate of oxidation of exogenous glucose [5].

A decreased thermic response has also been reported in obese subjects after a mixed meal [6], but not after a protein meal [7]. Overfeeding with fat caused a much smaller response in obese subjects than lean ones [8], and a single fat meal has been reported to give virtually no thermic response in obese subjects, but quite a large one in lean subjects [9].

To test the hypothesis that the thermic response to a meal is reduced in obesity we have investigated this response in lean and obese individuals to isoenergetic meals of protein, carbohydrate and fat. We have also measured the insulin response and the rate of exogenous glucose oxidation.

Subjects and methods
Subjects
The subjects were healthy, normotensive and euthyroid. Five were lean (age 31.4 ± 9.6 years, weight 60.1 ± 4.9 kg, $W/H^2$ 21.3 ± 1.2) and five
were obese (age 37.8 ± 13.3 years, weight 100.6 ± 17.5 kg, \( WH^2 \) 38.7 ± 6.4). In each group there were four women and one man. The protocol was approved by the Northwick Park Hospital Ethical Committee.

**Thermic response to meals**

Subjects were studied in a metabolic ward after an overnight fast of 12-14 h. The diet for the 2 days before the test contained at least 250 g of carbohydrate. Resting oxygen consumption and carbon dioxide production were measured with the subject in a supine position and in a thermoneutral environment, by using a ventilated hood system [10]. After 30 min of steady baseline measurements one of the following four meals (each 500 ml in volume) was given through a drinking straw, and indirect calorimetry was continued for another 157.5 min: carbohydrate (BDH, AnalaR glucose, 1.25 MJ, 300 kcal), protein (Maxiprot, 1.25 MJ, 300 kcal), fat (double cream, 1.25 MJ, 300 kcal) or control solution (fruit flavour of choice with sweetener in water, 0 MJ, 0 kcal).

**Plasma assays**

Blood samples were drawn from an intravenous cannula before the meal, and at 30 min intervals for 2 1/2 h after the meal, and assayed for insulin by the Amersham radioimmunoassay kit, and for glucose by autoanalyzer.

**Exogenous glucose oxidation**

We have used AnalaR glucose, derived from maize starch, as the carbohydrate meal in the present study. Glucose from this source has a sufficiently high \(^{13}\)C content to permit its oxidation to be monitored in human subjects via expired \(^{13}\)CO\(_2\) [11]. Expired air samples were collected before, and at 30 min intervals for 6 h after, the meal. The enrichment of \(^{13}\)CO\(_2\) in the expired air was measured by isotope-ratio mass spectrometry [12], and corrected for \(^{18}\)O content [13]. Since the rate of carbon dioxide production was known it was possible to calculate the cumulative rate of oxidation of the exogenous glucose [14].

**Statistical methods**

The significance of the difference between mean values for lean and obese subjects was compared by unpaired t-test.

**Results**

**Thermic response to meals**

The oxygen consumption of the lean and obese subjects before and after carbohydrate, protein and fat meals are shown in Figs. 1, 2 and 3. The baseline \( O_2 \) consumption was significantly greater (\( P < 0.02 \)) for the obese group than the lean group before each of the three test meals. However, when the response to the meal was calculated either as an absolute increase in oxygen consumption, or as a percentage increase over the baseline, there were no significant differences between the two groups.

In both groups of subjects the thermic response to the protein meal was significantly greater than that to isoenergetic amounts of carbohydrate or fat (\( P < 0.01 \)). When the increase in energy expenditure over baseline is expressed as a percentage of the energy value of the meal the response to

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**Fig. 1.** Baseline metabolic rate (mean ± SD) before, and increase in metabolic rate after, a meal of carbohydrate supplying 1.25 MJ.
Thermic response to meals

37henic response to meals calorimetry was discontinued, the response after 10-protein and fat was still near the peak value, whereas after carbohydrate the peak was reached 29-at about 45 min, and thereafter the oxygen uptake decreased. After the control (acaloric) meal there was no significant change in metabolic rate from baseline values during the 157.5 min of measurement.

Glucose tolerance and insulin response

The change in plasma glucose in the lean and obese groups after the glucose meal is shown in Fig. 4. None of the obese group was diabetic, since fasting glucose was less than 11 mmol/l at 2 h after a 75 g oral glucose load. However, the area under the curve of plasma glucose for the obese group was 426 mmol·l⁻¹·min, which was significantly greater than 216 for the lean group (t = 2.31, P < 0.05). Fig. 5 shows the plasma values in lean and obese groups after the meal of carbohydrate supplying 1.25 MJ.
and obese subjects before and after each of the three test meals. The fasting insulin concentration in the obese group (20.7 μ-units/ml) was significantly higher than that in the lean group (12.9 μ-units/ml; t = 2.85, P < 0.01), but the responses to the fat meal did not significantly differ between the two groups.

**Exogenous glucose oxidation**

The cumulative rate of glucose oxidation, calculated from the rate of $^{13}$CO$_2$ production, is shown in Fig. 6. There was no significant difference between the lean and obese groups in this respect: at 4 h after the glucose meal both lean and obese groups had oxidized 20% of the oral load (i.e. 15 g of exogenous glucose).

**Discussion**

Every investigation of the thermic response of groups of lean and obese subjects agrees on one point: that the resting metabolic rate of the obese group is higher than that of the lean group before the meal is given [4, 6, 15-17]. Our findings again confirm this observation.

We also confirm previous observations that the thermic effect after a meal of protein is larger than that for an isenergetic meal of either carbohydrate or fat for both lean and obese subjects [7, 9].

The point on which confusion and disagreement arises is the difference between lean and obese subjects in thermic response to a meal of carbohydrate or fat. The first report that obese subjects had a reduced response to a carbohydrate meal was by Pittet et al. [4]. They used a glucose load of 50 g, and demonstrated an increase in metabolic rate over the following 150 min of 23 kJ h$^{-1}$ m$^{-2}$ in a group of lean women, which was significantly greater (P<0.001) than the increase of 9 kJ h$^{-1}$ m$^{-2}$ in a group of obese women. In the light of subsequent work the response of the lean women (11.2% of the energy in the test meal) was unusually large. Later studies comparing the response of lean and obese groups to carbohydrate (type unspecified) [7], to sucrose and glucose [17] and to glucose (this paper) have failed to find a significant difference.

The Lausanne group [5] reported that the glucose intolerance of obese diabetic subjects was explained in part by reduced oxidation of exogenous glucose, and in a more recent paper [18] related the defective thermic response to glucose intolerance. The earlier paper [5] found no difference in thermic response between lean and non-diabetic obese subjects, but the later paper [18], which reports an extended series of patients, found decreased thermogenesis in both non-diabetic and diabetic obese subjects when compared with age-matched lean controls. However, this result is found only when the response is expressed as a percentage of the resting metabolic rate before the
meal, and not when expressed as a percentage of the energy in the glucose load. The obese diabetic subjects had the highest resting metabolic rate of the groups tested. The high resting metabolic rate of poorly controlled diabetic subjects is well documented, and seems to relate to their high rate of protein turnover [19].

To summarize: in failing to find a reduced thermic effect to a glucose meal in obese subjects we disagree with the original report of Pittet et al. [4] in Lausanne, but agree with workers in London [17] and Cambridge [7]. In diabetic subjects the interpretation of thermic effect is complicated by the high resting metabolic rate. There is no obvious difference in experimental design, which would explain the difference between the findings of Pittet et al. [4] and ourselves and the other workers cited.

The response of lean and obese subjects to a test meal of fat has been reported only in abstracts, and with very different protocols and results. Zed & James [8] studied eight obese subjects (116 kg) and eight lean subjects (50 kg) first on a diet supplying 10 MJ/day and then with a fat supplement adding another 4.2 MJ/day. The thermic effect was estimated from the change in 24 h energy expenditure, measured by whole body calorimetry. The observed increase in lean subjects was greater than in obese subjects (P<0.025). When the experiment was repeated by adding the fat supplement to a diet supplying 5 MJ/day the response was small and there was no difference between the lean and obese groups. This indicates that the difference arises only when the fat is fed in excess of energy requirements. However, the protocol rests on the improbable assumption that the diet of 10 MJ was equally adequate for subjects of 50 or 116 kg. If (as seems likely) the baseline diet was adequate for the lean subjects but not for the obese ones the difference in thermic response is easily explained without postulating a thermogenic defect in the obese subjects.

Swaminathan et al. [9] used a test meal of 1.68 MJ as vegetable oil, and measured the response of obese and lean subjects by indirect calorimetry for only 90 min after the meal. During this period their obese subjects actually showed a decrease in metabolic rate. It is not possible to comment in detail on this study, since there is no information about the time course of the change in metabolic rate, but 90 min seems too short a period to observe the response to fat. In our own study we have observed a slow but steady increase in metabolic rate after the meal in both lean and obese groups.

In our experience the thermic response to fat is small and slow compared with isoeenergetic meals of other nutrients, and therefore it is difficult to make technically satisfactory measurements. However, two indirect pieces of evidence throw doubt on the conclusion of Zed & James [8] that ‘thermic adaptation to meal feeding relates to its fat content’. If this is so it should be particularly difficult to make thin volunteers obese by feeding them fat, but the experience in the Vermont overfeeding study [20] was exactly the converse: fat supplements proved to be an unusually effective means to cause experimental obesity. The other study which bears indirectly on the problem is that of Hurni et al. [21] from Lausanne. They compared the effects of isoeenergetic diets containing either 92 g or 12 g of fat on the 24 h energy expenditure of normal lean men. There was no suggestion of a large thermic response to the high-fat diet: total energy expenditure was slightly greater on the low-fat diet. In the light of available evidence, therefore, we think it unlikely that the thermic effect of food is dependent on its fat content, or that lean subjects show a larger thermic response to fat than do obese subjects.

We have not investigated the response of lean and obese subjects to mixed meals, but since we have found no difference in thermic response to protein, carbohydrate or fat it is necessary to examine those reports of decreased thermogenesis in obese subjects after a mixed meal. A paper which is said to provide evidence for this reduced response is by Kaplan & Leveille [15], who gave four lean and four obese women a meal containing 3.4 MJ (largely contributed by 166 g of casein) which they ate in 1 h. Metabolic rate was measured hourly for the next 5 h. The increase in metabolic rate after the meal was not significantly different between the two groups (0.05 < P < 0.1) unless the result was divided by some function of body weight. A much better designed study was that of Shetty et al. [6], who compared the response to a mixed meal of lean, obese and formerly obese women. The meal was given in relation to the subjects' ideal body weights, so the lean subjects (90.6% of ideal body weight) received more food per kg than the obese (154% ideal) or post-obese (109% ideal). The lean subjects, in addition to being very lean, were selected for their claimed ability to eat ad libitum without weight gain, presumably because they had a great capacity for thermogenesis. The results showed a significantly greater thermogenesis in the lean group 90 and 120 min after the meal, but not at earlier stages. On examination of the data it is clear that the essential difference between the lean and obese groups lies in the resting metabolic rate, which was exceptionally low in the lean group (3.7 kJ/min compared with 4.3 kJ/min for our normal controls).
There is no doubt that some people, irrespective of their weight, have a larger thermic response to food than others, and people who say they can eat ad libitum without weight gain have been shown to have a larger response than those who do not make this claim [16]. Our normal controls were chosen for normal weight without conscious dieting, and for normal glucose tolerance, and not for exceptional thinness or thermogenic responsiveness. Probably this is the factor which contributes most to reconciling our results with those who report a diminished thermic response to food in obesity.

We expected differences between obese and lean subjects in their thermic response to meals of different composition, and hypothesized that these differences might have been explained by differences in insulin response and degree of insulin resistance. What happened was that we did not observe differences in thermic response to meals, but there were differences in plasma insulin. Before each type of meal the fasting insulin was higher in obese than in lean subjects (P < 0.01), and after the glucose load the increase in plasma glucose over 150 min was greater in the obese than lean subjects (P < 0.05), thus demonstrating relative glucose intolerance. There was no difference between lean and obese groups in the insulin response to the carbohydrate or fat meals, but after the protein meal the obese subjects showed a smaller insulin response than the lean subjects (r = 2.39; P < 0.05). It was suggested by Felber et al. [5] that the glucose intolerance of obese diabetic subjects was explained in part by reduced oxidation of exogenous glucose, but this effect was not seen at all in our non-diabetic, but glucose intolerant, obese subjects, since the rate of evolution of 13CO2 after the meal of 13C-labeled glucose was similar in both lean and obese groups.

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References