Fat and carbohydrate balances during adaptation to a high-fat diet

Steven R Smith, Lilian de Jonge, Jeffery J Zachwieja, Heli Roy, Tuong Nguyen, Jennifer C Rood, Marlene M Windhauser, and George A Bray

ABSTRACT

Background: Dietary fat contents are highly variable. Failure to compensate for the positive fat balance that occurs during the shift to a high-fat, low-carbohydrate diet by increasing energy expenditure or by decreasing food intake may result in the gain of fat mass.

Objective: The objective of this study was to investigate the time course of fat oxidation during adaptation to an isocaloric high-fat, low-carbohydrate diet.

Design: After a 5-d control diet, dietary fat was increased from 37% of energy to 50% of energy for 4 d in 6 healthy, young lean men. Respiratory quotient and substrate macronutrient oxidation and balance were measured in a respiratory chamber. Fasting concentrations of insulin, glucose, and triacylglycerol; maximal oxygen consumption (VO_{2max}) during treadmill exercise; and free-living energy expenditure were determined. Body fat was measured by dual-energy X-ray absorptiometry and visceral adipose tissue by computerized tomography.

Results: Compared with the baseline diet, the high-fat, low-carbohydrate diet resulted in positive fat and protein balances and a negative carbohydrate balance. Insulin concentration and the postabsorptive respiratory quotient were positively correlated with the fat balance during the high-fat, low-carbohydrate diet, whereas VO_{2max} during treadmill exercise was negatively related to fat balance. With use of stepwise regression, VO_{2max} was the best predictor of fat balance. There was a negative correlation between fat balance and carbohydrate balance ($r^2=0.88$).

Conclusion: Both baseline insulin concentration and VO_{2max} during treadmill exercise predict fat balance during the shift to a high-fat diet under isocaloric conditions. Am J Clin Nutr 2000;71:450–7.

KEY WORDS Respiratory chamber, physical fitness, insulin, macronutrient oxidation, dietary fat, fat oxidation, physical activity, macronutrient oxidation, fat balance, high-fat diet, obesity, men

INTRODUCTION

The prevalence of obesity is increasing at a rapid rate in Western societies and in societies that are adopting a Western pattern of food intake (1). Multiple factors are likely to be involved in the development of this epidemic, including increased dietary fat and decreased levels of physical activity. Public health efforts have emphasized the role of preventing weight gain as a means of preventing the complications of obesity.

High fat intakes (or low carbohydrate intakes) may also contribute to weight gain (1, 2). Dietary fat varies from day to day (3) and a shift from a high-carbohydrate to a high-fat diet results in a transiently positive fat balance (4–7). This occurs because it takes several days for fat oxidation to match the increased fat intake. After several days, fat oxidation rises to match fat intake and fat balance is achieved. Failure to compensate for the positive fat balance that occurs during the shift to a high-fat, low-carbohydrate diet by increasing energy expenditure (EE) or by a decrease in food intake results in the gain of fat mass.

Physical activity appears to be effective in preventing weight gain (8–10), although the exact mechanisms are not entirely clear. This may be partly because physical fitness is associated with an increase in the cellular machinery necessary to oxidize fat (11). In an earlier study, we examined the effects of both a high- and a low-carbohydrate diet in sedentary men and in 2 groups of athletes, 1 group with aerobic training and the other with weight training (12). In that study, there was a trend toward an effect of physical fitness level on fat oxidation after 7 d of a high-fat, low-carbohydrate diet. This suggested that differences in habitual activity or physical fitness may influence the adaptation to a high-fat, low-carbohydrate diet. Interpretation of substrate balances in that study was confounded because all of the men were in positive energy balance (12). Improved control of energy balance now allows us to reduce this difference between energy intake and EE to less than half that in the earlier study (13).

We hypothesized that the ability of an individual to adapt to a high-fat diet might be related to their level of physical fitness as assessed by maximal oxygen consumption (VO_{2max}). To test this hypothesis, we studied 6 sedentary, healthy young men in a metabolic chamber while changing their percentage of fat energy from 37% to 50% without changing the total daily energy intake.
SUBJECTS AND METHODS

Study volunteers
Six male volunteers were recruited via print advertising and completed comprehensive laboratory and physical examinations before signing an informed consent document. Men who were smokers, taking medications, or who performed > 2 h of weekly aerobic activity were excluded. The study protocol was approved by the local Institutional Review Board.

Protocol
Before the 5-d stay in the respiratory chamber, volunteers were fed a standard weight-maintenance diet that provided 37% of energy as fat for 4 d. The first day in the metabolic chamber the dietary fat content was also 37% of energy; this was raised to 50% for the next 4 d in the chamber.

Prediction of energy requirements before entry into the metabolic chamber
The resting metabolic rate (RMR, kJ/24 h) and respiratory quotient (RQ) of subjects in a semirecumbent position who had fasted overnight were measured with a metabolic cart by using a ventilated-hood system (model 2900Z metabolic cart; Sensormedics, Yorba Linda, CA). A triaxial activity monitor (Trirac model 3RD; Hemokinetics, Madison, WI) was used to estimate energy requirements and treadmill time within the metabolic chamber by using the following equation:

\[
\text{Expected sedentary EE in metabolic chamber} = \text{free-living EE by triaxial activity monitor} \times 0.85 \tag{1}
\]

This equation assumes a 15% decrease in EE from physical activity in the metabolic chamber when compared with free-living conditions (H Roy, J Lovejoy, unpublished observations, 1996). This estimate of total daily EE (TDEE) was used to calculate the treadmill time needed to achieve daily EE of 1.4 × RMR with use of equation 2.

\[
\text{Treadmill time (min)} = \frac{[\text{desired TDEE (kJ/24 h)} - \text{expected sedentary EE in metabolic chamber}]}{\text{exercise EE (4.83 km/h, or 3 mph) and 3% incline (kJ/min)}} \tag{2}
\]

The energy cost of physical activity was calculated by measuring VO2 with a Sensormedics metabolic cart (Vmax series 29) during treadmill walking under conditions similar to those used for exercise in the metabolic chamber. Briefly, volunteers were allowed to warm up by walking on the treadmill at 4.8 km/h and a 0% incline for 2 min. The treadmill speed was then set at 4.8 km/h and the incline raised to 3% and EE was measured continuously for the next 10 min. This EE was then used to calculate exercise time in the chamber as described above. VO2max was measured during exercise treadmill testing to exhaustion at the same visit and using the same equipment.

General chamber protocol and maintenance of energy balance
Volunteers left the chamber at 0730 each morning and reentered the chamber each morning before breakfast at 0900. Three meals were provided at scheduled intervals and exercise on the treadmill was prescribed at 4.8 km/h and a 3% incline to keep EE at the targeted level as described above. Lights were turned out at 1030. At 0700, the volunteers were awakened and at 0730 the volunteers left the chamber for 90 min. Between 0730 and 0900, the volunteers were allowed to bathe; however, physical activity was otherwise limited. The EE while outside the chamber was extrapolated from the EE readings obtained from 0900 to 1030. At the end of each day, EE was compared with energy intake to estimate energy balance. For the purposes of this interim calculation, metabolizable energy intake was estimated as 90% of the total daily energy intake. On the basis of the interim energy-balance result, 3 options were available. If the energy balance was <418 kJ (100 kcal), energy intake and treadmill time were not changed. If the energy balance was positive, energy intake was decreased, treadmill time was increased, or both to move the volunteer toward energy balance. If the energy balance was negative, energy intake was increased, treadmill time was decreased, or both to move the volunteer toward energy balance.

Body composition
Body composition was measured by dual-energy X-ray absorptiometry (DXA) using a Hologic model QDR 2000 apparatus (Hologic, Waltham, MA). Measurement of visceral adipose tissue was performed with a GE High-Speed CT scanner (GE Medical Systems, Waukesha, WI) and analyzed by using an off-scanner image analysis program (ANALYZE, version 7.5; CNSoftware, London). Body weight was measured each day before entry into the metabolic chamber and on completion of the 5-d metabolic chamber stay.

Design of metabolic diets
Diets were designed to provide either 37% or 50% of energy as fat. In designing the diets, composites were analyzed by the Food Chemistry Laboratory at Pennington Biomedical Research Center and adjusted accordingly. Protein content was fixed at 15% of energy and carbohydrate at 48% and 35% of energy for the low- and high-fat diets, respectively. The ratio of polysaturated to saturated fatty acids was similar for both of the diets at 0.7.

Calculation of energy and macronutrient balances
EE and substrate oxidations were calculated from (VO2, carbon dioxide consumption, and urinary nitrogen by using the equations of Acheson et al (14). The Acheson-calculated macronutrient oxidations (in g) were converted to kilocalories by using the Atwater factors (4.442, 4.183, and 9.461 kcal/g for protein, carbohydrate, and fat, respectively) and multiplied by 4.189 to convert kilocalories to kilojoules. For energy balances presented in the Results section, fecal energy was measured by collection of carmine red- and charcoal-marked fecal samples and bomb calorimetry of an aliquot from a 4-d composite. Urine was collected for each 24-h period and nitrogen was measured in each sample to calculate protein oxidation. For each volunteer and for each day in the chamber, duplicate meals were prepared and sent to the Food Chemistry Laboratory for analysis. The values for energy, fat, carbohydrate, and protein were then subtracted from the macronutrient oxidation values to calculate energy and macronutrient balances for each day. When measured on 4 occasions after a 4-d isonenergetic outpatient diet providing 37% fat, 14% protein, and 49% carbohydrate, the within-subject, repeated-measures CV for the 24-h RQ measured in our respiratory chamber was 1.7%.
Analytic methods

Urinary nitrogen was measured by using pyrochemiluminescence on an automated nitrogen analyzer (model 735; Antek Instruments, Houston). Urinary creatinine was measured by using the Jaffe rate reaction on a Synchron CX7 apparatus (Beckman Instruments, Brea, CA). Fecal samples were collected, weighed, and homogenized with an equal volume of water. After homogenization, <50 g fecal homogenate was freeze-dried and stored in an airtight container. Samples were weighed before and after freeze-drying. On the day of testing, the dried fecal material was compressed into a pellet (0.5–1 g) and analyzed for total energy content by using an oxygen bomb calorimeter (model 1241; Parr Instrument Company, Moline, IL).

Food composites were collected, weighed, homogenized, and frozen at −20°C until analyzed. Composites were analyzed for moisture, protein, fat, and ash, and carbohydrates were determined by difference. Moisture was analyzed by using a Labwave 9000 microwave oven (CEM, Matthews, NC). Protein was analyzed by using a combustion method on a nitrogen analyzer (Series II 2410; Perkin-Elmer, Norwalk, CT). Ash was measured by using an MAS 7000 microwave muffle furnace (CEM). Carbohydrate was calculated as 100 – (ash + protein + fat + moisture). Energy content was determined by using the following factors: 9 kcal/g fat, 4 kcal/g protein, and 4 kcal/g carbohydrate. These factors give total daily energy values that are equivalent to those determined by bomb calorimetry on identical samples (data not shown). Kilocalories were then converted to kilojoules by using 4.189 kJ/kcal as the conversion factor.

Statistical methods

Data were analyzed and graphed by using STATVIEW for WINDOWS and SUPERANOVA for Macintosh (both programs from SAS Institute, Cary, NC). A Bonferroni-Dunn correction was used as the post hoc contrast for the repeated-measures analysis of variance ANOVA).

RESULTS

The study population included healthy, but sedentary, young men with similar anthropometric characteristics (Table 1). A factor of 1.4 × resting EE was used to calculate energy intake. As shown in Figure 1, energy intake was actually closer to 1.5 × RMR. This was because the metabolizable energy content of the diet was closer to 93% than to 90%, which was used to predict energy requirements (see Eqs 1 and 2 in Methods). The diet composition measured in the laboratory is shown in Table 2. Overall,

![Image of Figure 1](https://example.com/figure1.png)

**FIGURE 1.** Mean (±SEM) ratios of daily metabolizable energy intake (EI: food energy – fecal energy) to resting metabolic rate (RMR) measured by indirect calorimetry, ratios of daily energy expenditure (EE) in the metabolic chamber to RMR measured by indirect calorimetry, and daily energy balances (metabolizable EI – EE) at baseline (B) and on days 1–4 of a high-fat, low-carbohydrate diet. n = 6.
dietary fat and carbohydrate intakes were similar to the target values. EEIs during the 5 d in the respiratory chamber are also shown in Figure 1. Energy intake was closely matched to EE (Table 3). Energy balance on days 2 and 3 was <800 kJ/d. The rise on day 4 reflected an uncompensated decrease in EE.

The increase in dietary fat resulted in the expected fall in non-protein RQ (npRQ) (Figure 2; P < 0.05 by repeated-measures ANOVA). The individual values for each chamber day are also presented in Figure 2. The interindividual variability in the rate of change in npRQ was large. It is notable that one individual did not appear to increase fat oxidation under sedentary conditions, as evidenced by a lack of change in npRQ (Figure 2; ○; bottom panel).

Daily macronutrient balances are shown in Table 4. As expected from the significant changes in npRQ (Figure 2), there was a trend toward an increase from baseline in fat balance when subjects ate the isocaloric high-fat diet. Carbohydrate balance became negative during the first day of isoenergetic high-fat feeding and remained negative for the remainder of the 4 d of the high-fat diet. Nitrogen balance became positive during the high-fat diet. Protein oxidation decreased as a result of isoenergetic high-fat feeding (P < 0.05 for comparison of baseline fat balance to that for days 1, 2, 3, and 4; Table 4).

Next, we explored the sources of interindividual variability in fat balance during high-fat feeding under sedentary conditions. Free-living V̇O₂max, free-living TDEE estimated by a triaxial activity monitor and expressed as a ratio to RMR, postabsorptive RQ, body mass index, percentage fat by DXA, lean body mass, visceral adipose tissue, and fasting insulin, fasting glucose, and triacylglycerol concentrations were tested for significant correlation with the cumulative fat balance (Table 5). Fasting insulin concentration and postabsorptive RQ were positively related to fat balance, whereas V̇O₂max was negatively related to the fat balance during the high-fat feeding period (Figure 3).

In an attempt to determine the best correlate of fat balance, insulin concentration, V̇O₂max, and postabsorptive RQ were entered into a stepwise multivariate regression with fat balance during high-fat feeding as the dependent variable. V̇O₂max was the only significant correlate of fat balance (P < 0.05, r² = −0.873). After adjustment for V̇O₂max, there was no significant correlation between insulin concentration or postabsorptive RQ and fat balance. The relation between cumulative fat balance and carbohydrate balance over the 4-d feeding period is shown in Figure 4. There was no relation between fat balance and either protein or energy balance or between protein balance and carbohydrate balance (data not shown).

### DISCUSSION

In this study, we showed that lean, sedentary young men differed in their response to a diet that is lower in carbohydrate and higher in fat than their usual diet while living in a respiratory chamber for 5 d. Some men came closer to achieving fat balance than did others. Nitrogen balance also became positive when the subjects ate the higher-fat diet. Baseline insulin concentrations, postabsorptive RQ, and V̇O₂max were predictors of the differences in fat oxidation in response to the high-fat diet.

These data can be viewed from the perspective of either carbohydrate balance or fat balance. Carbohydrate stores and dietary carbohydrate may provide 600 g carbohydrate, which is tiny compared with the 10 kg of fat stored in the adipose tissue of the young men who were the subjects of this study. When carbohydrate in the diet was reduced from 48% to 35% of energy on the second day in the respiratory chamber, there was a rapid reduction in carbohydrate oxidation that reduced carbohydrate balance to a mean value of −20 g (=320 kJ) on days 1 and 2. Carbohydrate balance was again achieved by day 4. However, there was considerable variation in the completeness of this adaptation.

A high baseline RQ, ie, increased carbohydrate oxidation, has been identified as a predictor of weight gain or weight regain in several studies (15–18). In our study, the individuals with the highest baseline RQs also had the highest baseline insulin concentrations and lowest baseline V̇O₂max values. The individuals who adapted to the low-carbohydrate diet via reduced carbohydrate oxidation most effectively had the lowest insulin concentrations, suggesting that a low level of insulin resistance may be a factor in determining the response to high-fat diets. Insulin resistance may be associated with an inability to shut down

### TABLE 2

<table>
<thead>
<tr>
<th></th>
<th>Standard diet</th>
<th>High-fat diet</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Measured</td>
<td>Target</td>
</tr>
<tr>
<td>Fat (% of energy)</td>
<td>36.8</td>
<td>37</td>
</tr>
<tr>
<td>Carbohydrate (% of energy)</td>
<td>49.4</td>
<td>48</td>
</tr>
<tr>
<td>Protein (% of energy)</td>
<td>13.7</td>
<td>15</td>
</tr>
<tr>
<td>P:S</td>
<td>0.7</td>
<td>0.7</td>
</tr>
</tbody>
</table>

1 Values were measured from duplicate meals prepared by the metabolic kitchen and analyzed by the Food Chemistry Laboratory (see Methods for details), except for the P:S (ratio of polyunsaturated to saturated fatty acids), which was calculated from database values.

#### TABLE 3

<table>
<thead>
<tr>
<th>Study day</th>
<th>Energy intake</th>
<th>Energy expenditure</th>
<th>Fecal energy</th>
<th>Energy balance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>kJ/d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>11257 ± 450¹</td>
<td>9334 ± 265</td>
<td>714.5</td>
<td>1209 ± 356</td>
</tr>
<tr>
<td>Day 1</td>
<td>11239 ± 353</td>
<td>9692 ± 463</td>
<td>714.5</td>
<td>832 ± 487</td>
</tr>
<tr>
<td>Day 2</td>
<td>11327 ± 483</td>
<td>9828 ± 453</td>
<td>714.5</td>
<td>784 ± 181</td>
</tr>
<tr>
<td>Day 3</td>
<td>11484 ± 479</td>
<td>10001 ± 365</td>
<td>714.5</td>
<td>768 ± 192</td>
</tr>
<tr>
<td>Day 4</td>
<td>11600 ± 515</td>
<td>9774 ± 413</td>
<td>714.5</td>
<td>1110 ± 220</td>
</tr>
</tbody>
</table>

¹ Measured directly on a composite of fecal material collected at baseline and on days 1, 2, and 3. Because a fecal sample was not available for day 4, fecal energy for day 4 was assumed to be equal to mean daily fecal energy from the 4-d period encompassing baseline and days 1–3.

² x ± SEM; n = 6.
TABLE 4

Macronutrient intake, oxidation, and balance

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Carbohydrate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intake</td>
<td>5560 ± 234</td>
<td>4368 ± 168</td>
<td>4158 ± 184</td>
<td>4195 ± 152</td>
<td>4209 ± 119</td>
</tr>
<tr>
<td>Oxidation</td>
<td>4871 ± 416</td>
<td>4902 ± 422</td>
<td>4700 ± 398</td>
<td>4534 ± 360</td>
<td>4401 ± 391</td>
</tr>
<tr>
<td>Balance</td>
<td>689 ± 401</td>
<td>−535 ± 386</td>
<td>−542 ± 364</td>
<td>−340 ± 216</td>
<td>−193 ± 414</td>
</tr>
<tr>
<td><strong>Fat</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intake</td>
<td>4153 ± 189</td>
<td>5347 ± 188</td>
<td>5536 ± 221</td>
<td>5711 ± 313</td>
<td>5749 ± 435</td>
</tr>
<tr>
<td>Oxidation</td>
<td>2696 ± 281</td>
<td>3398 ± 171</td>
<td>3577 ± 296</td>
<td>3964 ± 161</td>
<td>3761 ± 186</td>
</tr>
<tr>
<td>Balance</td>
<td>1457 ± 368</td>
<td>1948 ± 257</td>
<td>1598 ± 254</td>
<td>1747 ± 348</td>
<td>1988 ± 469</td>
</tr>
<tr>
<td><strong>Protein</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intake</td>
<td>1544 ± 60</td>
<td>1524 ± 53</td>
<td>1633 ± 89</td>
<td>1578 ± 88</td>
<td>1642 ± 79</td>
</tr>
<tr>
<td>Oxidation</td>
<td>1790 ± 149</td>
<td>1399 ± 136</td>
<td>1561 ± 146</td>
<td>1509 ± 133</td>
<td>1623 ± 70</td>
</tr>
<tr>
<td>Balance</td>
<td>−246 ± 110</td>
<td>126 ± 131</td>
<td>72 ± 117</td>
<td>69 ± 51</td>
<td>18 ± 66</td>
</tr>
</tbody>
</table>

1 $\pm$ SEM; n = 6.
2 Significant effect of time, $P < 0.05$ (repeated-measures ANOVA).
3 Significantly different from baseline, $P < 0.05$ (repeated-measures ANOVA).
4 Significant linear trend of reduction in carbohydrate oxidation over time, $P < 0.05$.
5 Effect of time, $P = 0.15$.

**FIGURE 2.** Mean (±SEMs) and individual (bottom panel) changes in 24-h nonprotein respiratory quotient (npRQ) during adaptation to an isoenergetic high-fat (low carbohydrate) diet expressed as for the high-fat, low-carbohydrate diet for 4 d. Dietary fat at baseline (B) was 37% of energy. *Significantly different from baseline, $P < 0.05$. The arrow represents the expected change in RQ with the high-fat diet if fat oxidation and fat intake were equal. n = 6.

Fat oxidation in muscle can be modulated by several factors. Exercise increases fat oxidation in muscle by increasing the activity of lipoprotein lipase (11) and carnitine O-palmitoyltransferase I (23) and the number of mitochondria (24). Physical fitness is correlated with the concentrations of enzymes needed to oxidize fatty acids (11). Collectively, these processes enhance the availability of fatty acids, their transport into mitochondria, and their rate of oxidation by muscle.

When interpreting the current data from the viewpoint of fat oxidation, we note that 76% of the variance in fat balance could be accounted for by the $\dot{V}O_2\text{max}$. In the absence of significant hepatic glucose output, insulin secretion, and consequently, glucose oxidation (19). This would be consistent with the observations of Sidossis et al (20) that the rate of glycolytic flux determines fatty acid oxidation (20). Colberg et al (21) suggested that central adipose tissue or insulin resistance contributed to decreased fat oxidation in skeletal muscle. In our study, the higher insulin concentrations, which may reflect insulin resistance, were associated with the highest cumulative fat balances, consistent with this line of reasoning.

An alternative interpretation of the control mechanism for adaptation to high-fat diets is to view these results from the perspective of fat oxidation. Carbohydrate balance and fat balance had a strong inverse relation ($r^2 = 0.86$), as would be expected at energy balance. Fat oxidation increased when the subjects were eating the high-fat diet, but there was considerable individual variability in the response. This view holds that the machinery that oxidizes fat is either 1) not sufficient to match the fat load, 2) not activated in a timely fashion by a signal (or signals) necessary to oxidize fat, or 3) that intracellular fatty acid availability is decreased. Flatt (4) has argued that one mechanism for an adaptation to high-fat diets is an increase in fat stores until fat oxidation rises to meet intake. The correlation of body fat with fat oxidation supports this concept. Short-term supplementation of a standard diet with fat results in fat storage because fat oxidation only slowly adapts to the higher-fat, lower-carbohydrate diet (22). As noted in our studies and in those of Schrauwen et al (7), several days are required to achieve fat balance.

Fat oxidation in muscle can be modulated by several factors. Exercise increases fat oxidation in muscle by increasing the activity of lipoprotein lipase (11) and carnitine O-palmitoyltransferase I (23) and the number of mitochondria (24). Physical fitness is correlated with the concentrations of enzymes needed to oxidize fatty acids (11). Collectively, these processes enhance the availability of fatty acids, their transport into mitochondria, and their rate of oxidation by muscle.

When interpreting the current data from the viewpoint of fat oxidation, we note that 76% of the variance in fat balance could be accounted for by the $\dot{V}O_2\text{max}$. In the absence of significant
cardiovascular disease, \( \dot{V}\!O_2 \text{max} \) is a reasonable estimate of the oxidative capacity of skeletal muscle—creating a link between fitness, fat oxidation potential, and adaptation to high-fat diets. Genetics, sex, habitual level of physical activity, body weight, and age are some of the factors known to modulate \( \dot{V}\!O_2 \text{max} \) (25).

Other neural or endocrine mechanisms may also increase fat oxidation. When healthy young men were treated with a synthetic \( \beta \)-3 agonist, there was a decrease in 24-h RQ (26). It is possible that the sympathetic nervous system, acting through the \( \beta \)-3 adrenoreceptor, is a component in the regulation of fat or carbohydrate oxidation. Further work in this area is warranted.

Previous studies identified several factors that alter the rate of adaptation to high-fat diets. First, in young women who were restrained eaters, fat balance was more positive after 3 d of eating a isoenergetic high-fat diet than in nonrestrained women eating the same diet (27). Second, obesity may also play a role. Although lean individuals eventually adjust fat oxidation to match fat intake, obese individuals adapt slowly to high-fat feeding (2). Obese subjects showed no relation between the amount of dietary fat consumed and the amount of fat oxidized. On the other hand, lean subjects, like those in our study and the study of Schrauwen et al (7), increased their fat oxidation to match intake. These interindividual differences may translate into differences in weight gain over time when individuals are exposed to a high-fat diet. Thomas et al (2) pointed out that “it is possible that individuals differ in how quickly equilibrium between food quotient (FQ) and respiratory quotient (RQ) is achieved...and that time course differences may be important in determining susceptibility to dietary obesity.”

Impaired fat oxidation is a characteristic of the formerly obese population. Astrup et al performed a series of studies in which the adaptation to a high-fat diet was studied in formerly obese women. These women, who had reduced their weight to within 10% of ideal body weight and had been weight stable for \( \geq 2 \) mo, were compared with age- and BMI-matched never-obese women. The rate of fat oxidation was then measured acutely after a high-fat (50% of energy) meal (28) or after a 3-d high-fat diet (29, 30). Under both the acute and chronic conditions, fat oxidation was suppressed in the formerly obese women. This suggests that these women had a low capacity to oxidize fat.

High-fat foods are energy dense and palatable, potentially increasing their overall consumption (31, 32). In the present study, altered intake was not permitted because the experimenters manipulated EE and energy intake. When diets with different fat contents are fed covertly, adaptation is slow (33). However, when subjects are familiar with the available foods dietary adaptation may be more effective (34) and may also be related to the perceived carbohydrate content of the foods. One component of the adaptation to energy-dense and highly palatable foods may be

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**TABLE 5**

Simple correlation coefficients \((r)\) between baseline population characteristics and cumulative fat balance \((g/4 \text{ d})\) over the 4-d feeding period

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>(r)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\dot{V}!O_2 \text{max} ) (mL \cdot kg body wt (^{-1} \cdot \text{min}^{-1}))</td>
<td>-0.873</td>
<td>0.02</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>0.579</td>
<td>0.25</td>
</tr>
<tr>
<td>VAT (cm(^2))</td>
<td>-0.203</td>
<td>0.72</td>
</tr>
<tr>
<td>Fasting insulin (pmol/L)</td>
<td>0.838</td>
<td>0.03</td>
</tr>
<tr>
<td>Fasting triacylglycerol (mmol/L)</td>
<td>0.176</td>
<td>0.7</td>
</tr>
<tr>
<td>Postabsorptive respiratory quotient</td>
<td>0.758</td>
<td>0.08</td>
</tr>
<tr>
<td>TDEE:RMR</td>
<td>-0.248</td>
<td>0.66</td>
</tr>
</tbody>
</table>

\(\dot{V}\!O_2 \text{max},\) maximal oxygen consumption; VAT, visceral adipose tissue; TDEE, total daily energy expenditure; RMR, resting metabolic rate.

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**FIGURE 3.** Regression plot of the relation of cumulative fat balance to the fasting insulin concentration, postabsorptive respiratory quotient (RQ), and maximal oxygen consumption \((\dot{V}\!O_2 \text{max})\) for each of the 6 male volunteers. \(P < 0.05\) for fasting insulin concentration and \(\dot{V}\!O_2 \text{max}\); \(P = 0.08\) for fasting insulin concentration and postabsorptive RQ.
the rate at which carbohydrate oxidation is inhibited and the rate at which fat oxidation can be increased. The present study suggests that this response time is highly variable.

Genetic factors may also play a role in these differential responses to lower-carbohydrate diets. Several animal models have been used to map genes related to the susceptibility to increases in body fat when animals eat a high-fat diet (35).

Although the individual genes have not been identified (36), the fact that these differences exist in animals is consistent with the observations of individual differences noted here.

In summary, this study showed a delay in the rise in fat oxidation when healthy lean young men were shifted from a 37%-fat diet to a 50%-fat diet. Individuals in whom carbohydrate oxidation decreased had a less positive fat balance during the shift to a high-fat diet expressed as the cumulative carbohydrate balance (MJ/d) = 6.4 – 0.77 × cumulative carbohydrate balance ($r^2 = 0.88, P < 0.05$).

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REFERENCES


