# Relationship of dietary saturated fatty acids and body habitus to serum insulin concentrations: the Normative Aging Study[1-3]

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**ABSTRACT** The purpose of this study was to examine the relationship of body mass index, abdomen-hip ratio, and dietary intake to fasting and postprandial insulin concentrations among 652 men aged 43–85 y, followed in the Normative Aging Study. Log-transformed fasting insulin was significantly associated with body mass index, abdomen-hip ratio, total fat energy, and saturated fatty acid energy, with correlation coefficients ranging from 0.14 for total fat to 0.45 for body mass index. When multivariate models were used, body mass index, abdomen-hip ratio, and saturated fatty acid intake were statistically significant independent predictors of both fasting and postprandial insulin concentrations, after age, cigarette smoking, and physical activity were adjusted for. If saturated fatty acids as a percentage of total energy were to decrease from 14% to 8%, there would be an 18% decrease in fasting insulin and a 25% decrease in postprandial insulin. These data suggest that overall adiposity, abdominal obesity, and a diet high in saturated fatty acids are independent predictors for both fasting and postprandial insulin concentrations. *Am J Clin Nutr* 1993;58:129–36.

**KEY WORDS** Hyperinsulinemia, abdomen-hip ratio, saturated fatty acid

## Introduction

Obesity is a recognized risk factor for the development of ischemic heart disease (1), hypertension (2, 3), stroke (4), total cardiovascular mortality (5, 6), and non-insulin-dependent diabetes mellitus (7). Hyperinsulinemia, which frequently accompanies obesity, has also been associated with risk of hypertension (8–10) and coronary artery disease (11). Although the hyperinsulinemia of obesity is imperfectly understood, many factors including insulin resistance and diet have been implicated in this relationship. Because hyperinsulinemia has emerged as an independent risk factor for cardiovascular disease, factors that affect insulin concentrations are of considerable interest. Once identified, these factors may be amenable to modification for therapeutic benefit.

Evidence has accumulated that abdominal adiposity, characterized by a high abdomen-hip circumference ratio, is associated with insulin resistance and hyperinsulinemia (12, 13). This is especially true for viceroabdominal obesity (13). The effect of dietary intake is less certain, although Grey and Kipnis (14) noted > 20 y ago that short-term carbohydrate feeding increased insulin concentrations in obese subjects. In addition, experimental studies in animals indicate that diets high in fat lead to the induction of insulin resistance and hyperinsulinemia (15).

In the present study the relationship of dietary intake and body-fat distribution to fasting and postprandial insulin concentrations was examined among a group of 652 nondiabetic male participants in the Normative Aging Study.

## Methods

The Normative Aging Study cohort has been described in detail previously (16). Briefly, volunteers were screened at entry and individuals with chronic medical conditions, including hypertension, were excluded. However, obese individuals were not excluded. Participants were seen every 3–5 y for a comprehensive examination that included a medical history, a physical and anthropometric examination, electrocardiogram, chest x-ray, and blood and urine tests. The present investigation is based on a subgroup of 890 men who had regular follow-up examinations between February 1987 and May 1989. Twenty-seven percent (238 of 890 men) had to be excluded from the analysis for the following reasons: 131 men had missing insulin values; 11 had missing glucose values; 55 had incomplete anthropometric measurements, smoking data, or diet information; and 41 had diabetes (defined as fasting glucose concentrations > 7.7 mmol/L or postprandial concentrations > 11.1 mmol/L).

### Data collection

A series of anthropometric measurements were made on the right side of the body (17). Subjects were measured in undershorts

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and socks. Height was measured against a wall chart to the nearest 0.1 inch and converted to meters; weight was measured on a balance-beam scale to the nearest 0.5 pound and converted to kilograms. Abdominal circumference was measured in centimeters at the level of the umbilicus. Hip circumference was measured in centimeters at the greatest protrusion of the buttocks. Two indexes were calculated as follows: body mass index = weight/height$^2$ (kg/m$^2$) and abdomen-hip ratio = abdomen circumference-hip circumference.

Before the examination, participants were instructed to refrain from eating or drinking after midnight, and a fasting insulin measurement was obtained on the morning of the exam. A postprandial insulin measurement was obtained 2 h after a 100-g glucose load. Serum insulin concentrations were determined by a solid-phase $^{125}$I radioimmunoassay (Diagnostic Products Corporation, Los Angeles).

A self-administered semiquantitative food-frequency questionnaire, developed by Willett et al (18, 19), was used to assess the participant's food intake during the past year. This questionnaire yielded estimates of macro- and micronutrient intakes derived from the subject's report of frequency of intake for a given serving size of a list of food items and nutrient-composition tables published by the US Department of Agriculture (20). Questionnaires for subjects ($n$ = 5) with computed total energy-intake values outside the range of 2514–19 274 kJ (600–4600 kcal) were excluded before data analysis because of possible errors in filling out the food-frequency questionnaire.

Physical activity was assessed by using a scale derived by Paffenbarger et al (21). An activity score was calculated based on a self-report of the number of stairs climbed, blocks walked, and sport activities played on average per week.

Smoking information was obtained by an interviewer-administered smoking questionnaire. Individuals were categorized as current smokers, former smokers (according to their smoking status on the day of their exam), or never smokers. All protocols were approved by the Committee on Research Investigations of both Brigham and Women's Hospital and the Veteran's Administration Outpatient Facility.

## Data analysis

Data analysis was performed by using the *Statistical Analysis System* (SAS) (22). Fasting and postprandial insulin measurements and physical activity were logarithmically (natural log; ln) transformed because of the skewed distributions of these variables. The strength of the relationships between ln fasting and ln postprandial insulin and measures of body habitus and diet were examined by using Pearson product-moment correlation coefficients. Dietary variables used in the analyses included protein, carbohydrate, total fat, saturated fatty acid, animal fat, and vegetable fat. Nutrient densities for carbohydrate, fat, and protein were used in the regression analyses and were computed by dividing the nutrient values for the macronutrients by total energy (23). Total energy intake and saturated fatty acid intake were highly correlated. To ensure that the effect of saturated fatty acid was independent of the effect of total energy, a second analysis was performed by using the energy-adjusted method suggested by Willett (23) and Willett and Stampfer (24). Energy-adjusted saturated fatty acid intake was computed as the residuals from a regression model with saturated fatty acid as the dependent variable and total energy intake as the independent variable. A constant, the mean value for total energy intake, was added to the residuals because the residuals had a mean of zero. The energy-adjusted value of saturated fatty acid was then used in multivariate models, with and without total energy and total fat in the model.

Analysis of covariance was used to compare serum insulin concentrations by tertile of abdomen-hip ratio, body mass index, and saturated fatty acid, after adjustments were made for age, physical activity, and smoking status. The antilogs of the insulin values were then obtained; the values presented in the tables show the retransformed serum insulin measurements. Multiple-regression methods were used to determine the association of log-transformed fasting and postprandial insulin with measures of body mass index and abdomen-hip ratio and total and saturated fatty acid intake after adjustment was made for age, smoking status, and physical activity. Each dietary variable was adjusted for total energy intake.

## Results

Descriptive statistics for the study participants are presented in **Table 1.** Forty-one percent of the population was obese (body mass index $\geq$ 27; in kg/m$^2$). The subgroup of men who were excluded from the analyses were compared with the study participants to determine whether bias resulted from selective de-

TABLE 1
Characteristics of participants in the Normative Aging Study*

| | Value |
|---|---|
| Age (y) | 61.7 ± 7.9† |
| Weight (kg) | 82.1 ± 12.3 |
| Height (m) | 1.75 ± 0.06 |
| Body mass index‡ | 26.6 ± 3.4 |
| Abdomen circumference (cm) | 100.3 ± 8.9 |
| Hip circumference (cm) | 102.6 ± 6.9 |
| Abdomen-hip ratio | 0.97 ± 0.04 |
| Insulin (pmol/L) | |
| Fasting | 6.6 (63.71–69.45)§ |
| Postprandial | 330.8 (311.25–351.65) |
| Total energy intake | |
| (kJ/24 h) | 8416.03 ± 2677.41 |
| (kcal/24 h) | 2008.6 ± 639.0 |
| Glucose (mmol/L) | |
| Fasting | 5.5 ± 0.58 |
| Postprandial | 6.0 ± 1.54 |
| Total fat (% of total energy) | 30.3 ± 5.67 |
| Saturated fatty acid | |
| (percent of total energy) | 10.9 ± 2.71 |
| Physical activity | |
| (kJ/wk) | 4801.4 (4450.99–5179.99) |
| (kcal/wk) | 1143.2 (1059.76–1233.33) |
| Smoking status (%)‖ | |
| Never | 32.7* |
| Former | 57.3* |
| Current | 10.0* |

* n = 652.
† $\bar{x}$ ± SD.
‡ ln weight (kg)/height (m$^2$).
§ 95% confidence interval.
‖ Percent of total number of subjects.

pletion of the study sample. Subjects excluded because of missing values were significantly older (63.4 y; $P = 0.01$), weighed less (79.7 kg; $P = 0.03$), and were shorter (1.72 m; $P < 0.001$); they did not differ in any other characteristics.

Pearson product-moment correlations for ln fasting and postprandial insulin concentrations with measures of body habitus and diet are presented in **Table 2.** Correlation coefficients between ln fasting insulin and body mass index, abdomen circumference, abdomen-hip ratio, total fat, and saturated fatty acid were statistically significant and ranged from 0.14 ($P = 0.0001$) for total fat to 0.45 for body mass index ($P = 0.0001$). Similarly, correlation coefficients between ln postprandial insulin and body mass index, abdomen circumference, abdomen-hip ratio, total fat, and saturated fatty acid were statistically significant and ranged from 0.12 ($P = 0.001$) for total fat to 0.39 ($P = 0.0001$) for body mass index. The correlations among saturated fatty acid, total fat, body mass index, and abdomen-hip ratio were also examined. Correlation coefficients between saturated fatty acid and abdomen-hip ratio ($r = 0.08$; $P = 0.02$) and between total fat and body mass index were statistically significant ($r = 0.14$; $P = 0.0002$).

The degree to which abdomen-hip ratio, body mass index, and energy-adjusted saturated fatty acid intake were associated with serum insulin concentrations is presented in **Figures 1 and 2.** Mean values of fasting and postprandial serum insulin were adjusted for age, smoking, and physical activity but not for saturated fatty acid or body-habitus variables. Mean values for fasting serum insulin (pmol/L) were 56.0, 66.0, and 473.6 for the lowest to the highest tertile of abdomen-hip ratio, respectively (Fig 1). These results represent a 44% increase over the range of abdomen-hip ratio. Mean fasting insulin values increased 77.5% over the range of body mass index, and the tertile means from the lowest to the highest were 50.9, 63.9, and 90.4 pmol/L (Fig 1). Within tertiles of saturated fatty acid intake, adjusted for total energy, mean fasting serum insulin increased from the low to the middle tertile, with no further increase in the highest tertile (Fig 1); the means were 58.1, 71.8, and 71.0 pmol/L, respectively.

The mean value for saturated fatty acid intake as a percentage of total energy for the lowest tertile was 7.8% for the middle

TABLE 2
Pearson product-moment correlations for log-transformed fasting and postprandial insulin with measures of body habitus and diet*

| | Fasting | | Postprandial | |
|---|---|---|---|---|
| | Insulin | *P* | Insulin | *P* |
| Body mass index† | 0.45 | 0.0001 | 0.39 | 0.0001 |
| Abdomen circumference (cm) | 0.44 | 0.0001 | 0.35 | 0.0001 |
| Abdomen-hip ratio | 0.31 | 0.0001 | 0.29 | 0.0001 |
| Total energy intake (kJ/24 h) | −0.02 | 0.5940 | −.0004 | 0.9901 |
| Total fat (% of total energy) | 0.14 | 0.0001 | 0.12 | 0.001 |
| Saturated fatty acid (% of total energy) | 0.17 | 0.0001 | 0.16 | 0.0001 |
| Protein (% of total energy) | 0.03 | 0.3988 | −0.007 | 0.8422 |
| Carbohydrate (% of total energy) | −0.06 | 0.1070 | −0.06 | 0.1052 |

* $n = 652$.
† ln weight (kg)/height ($m^2$).

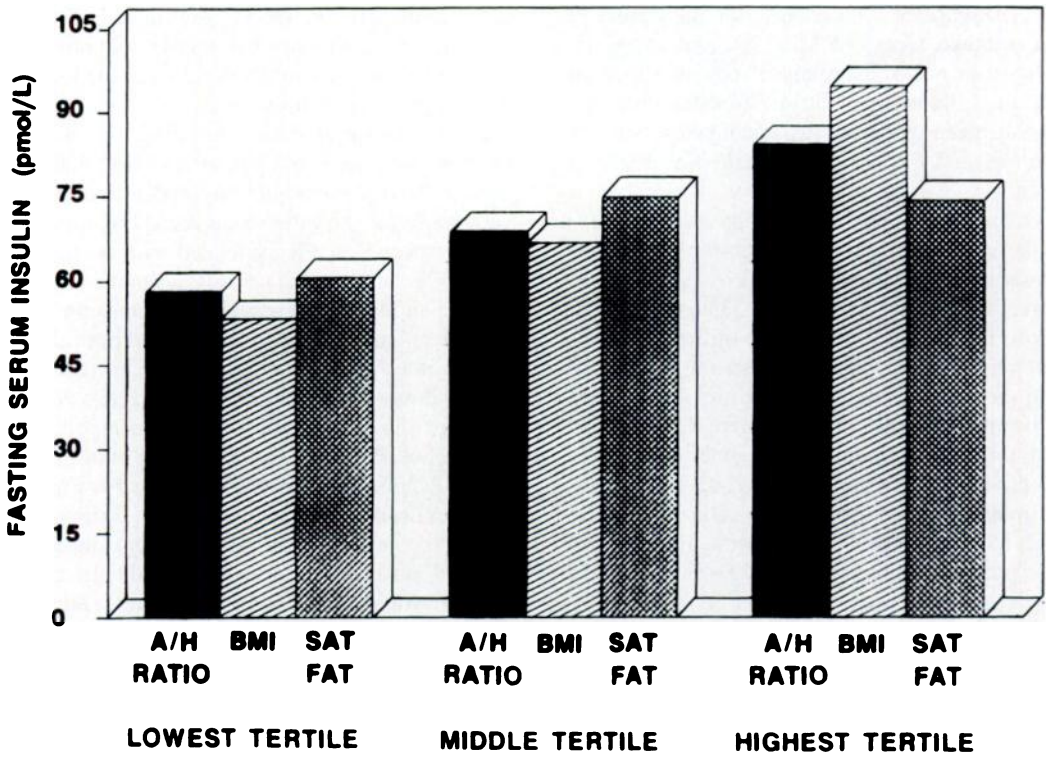


FIG 1. Mean fasting insulin values by tertiles of abdomen-hip ratio, body mass index, and saturated fatty acid intake (abscissa). Results are adjusted for age, smoking, and physical activity. ■, Abdomen-hip ratio; ▨, body mass index; and ▩, saturated fatty acid intake.

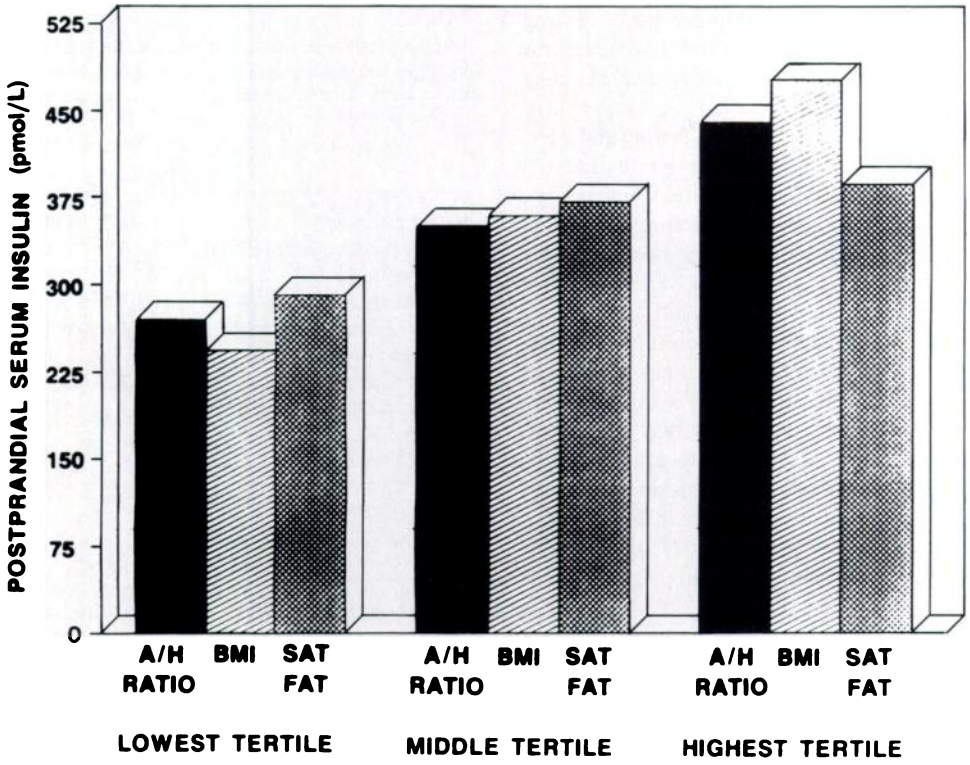


FIG 2. Mean postprandial serum insulin values by tertiles of abdomen-hip ratio, body mass index, and saturated fatty acid intake (abscissa). Results are adjusted for age, smoking, and physical activity. ■, abdomen-hip ratio; □, body mass index; and ▩, saturated fatty acid intake.

tertile 10.9%, and for the highest tertile 13.9%. The mean values of total fat as a percentage of total energy, for the tertiles of saturated fatty acid intake, were 24.8%, 30.7%, and 35.5%, respectively. Results from univariate analysis indicated that for the total group the mean unsaturated fatty acid intake was 19.4% of total energy intake, mean saturated fatty acid intake was 10.9% of total energy intake, and mean total fat intake was 30.3% of total energy intake.

For postprandial serum insulin, values increased from the lowest tertile to the highest tertile of abdomen-hip ratio, body mass index, and saturated fatty acid intake (Fig 2). The mean values for postprandial insulin were 258.3, 333.6, and 419.0 pmol/L for the low, middle, and high tertiles of the abdomen-hip ratio, respectively. Mean postprandial serum insulin increased 62% from the lowest to the highest tertile of abdomen-hip ratio. Mean postprandial insulin values were 232.5, 342.4, and 451.2 pmol/L for the low, middle, and high tertiles of body mass index, respectively, an overall increase of 95.5%. For saturated fatty acid intake, serum postprandial insulin values were 277.7, 353.7, and 368.8 pmol/L for the lowest, middle, and highest tertiles, respectively, comprising a 32.7% increase over the range.

Multiple linear regression was used to assess the relationship between fasting and postprandial insulin and measures of body habitus and diet. This analysis allowed for simultaneous control of all variables potentially influencing serum insulin concentrations. The outcome variables were ln fasting and ln postprandial insulin; predictor variables included age, smoking habit, body mass index, abdomen-hip ratio, physical activity, and saturated fatty acid as a percentage of total energy (**Table 3**). Abdomen-hip ratio ($P = 0.0005$) and saturated fatty acid ($P = 0.0072$) were significantly related to basal insulin after adjustment for age, smoking habit, body mass index, and physical activity. The regression model accounted for 23% of the total variance in the fasting insulin concentration.

The regression analysis examining the relationship between postprandial insulin and measures of body habitus and diet also showed that abdomen-hip postprandial insulin after adjustments were made for the other covariates. Log-transformed physical activity was negatively associated with postprandial insulin ($P = 0.0057$). The regression model accounted for 19% of the total variance in the postprandial insulin concentrations.

The relationship between fasting and postprandial insulin and several other dietary factors (ie, protein, simple and complex carbohydrates, vegetable fat, and alcohol) was also examined (data not shown). Except for the association of fasting insulin and alcohol ($P = 0.02$), the association of insulin and these other dietary factors was nonsignificant. Furthermore, saturated fatty acid remained significantly related to fasting and postprandial insulin in the regression models after adjustment for alcohol intake. When energy-adjusted saturated fatty acid was substituted for the nutrient density in the regression model, the results were similar to those in Table 3 (data not shown).

To ensure that the dietary effects on serum insulin were due to saturated fatty acid intake and not to total fat intake, we extended the regression models to include saturated fatty acid intake, total fat intake, and total energy. Saturated fatty acid intake remained borderline significant whereas total fat and total energy were not significant predictors of fasting ($P = 0.057$) or postprandial ($P = 0.07$) serum insulin.

TABLE 3
Regression analysis: relationship between log-transformed fasting and postprandial insulin and measures of body habitus and diet, adjusted for age, smoking, and physical activity

| Variables | Fasting insulin | | | Postprandial insulin | | |
|---|---|---|---|---|---|---|
| | $\beta$ | SE | $P$ | $\beta$ | SE | $P$ |
| Intercept | −1.1850 | 0.5132 | 0.0213 | −0.4755 | 0.7296 | 0.5148 |
| Age (y) | −0.00004 | 0.0025 | 0.9875 | 0.0048 | 0.0036 | 0.1872 |
| Smoking status | | | | | | |
| Current vs never | −0.0410 | 0.0740 | 0.5800 | −0.1205 | 0.1052 | 0.2527 |
| Former vs never | 0.0300 | 0.0438 | 0.4929 | 0.02090 | 0.0623 | 0.7365 |
| Body mass index* | 0.0613 | 0.0066 | 0.0001 | 0.0719 | 0.0095 | 0.0001 |
| Abdomen-hip ratio | 1.7133 | 0.4858 | 0.0005 | 2.4401 | 0.6906 | 0.0004 |
| Physical activity (kJ/wk) | −0.0174 | 0.0205 | 0.3961 | −0.0811 | 0.0292 | 0.0057 |
| Saturated fatty acid (% of total energy) | 2.0305 | 0.7532 | 0.0072 | 2.5917 | 1.0707 | 0.0158 |

* In weight (kg)/height ($m^2$).

To illustrate the degree to which saturated fatty acid and abdomen-hip ratio were associated with insulin concentrations, the means for the lowest and highest tertiles of abdomen-hip ratio at various saturated fatty acid intakes were used with the regression coefficients from the model in Table 3 to calculate predicted insulin concentrations. The population mean age, body mass index, physical-activity level, and nonsmoking category were used in the calculation of prediction. The insulin values given in Table 3 are retransformed values. Both predicted fasting and predicted postprandial insulin concentrations for individuals in the lowest tertile of abdomen-hip ratio increased from 5% saturated fatty acid intake (53.8 pmol/L for fasting insulin and 250.4 pmol/L for postprandial insulin) to 20% saturated fatty acid intake (72.5 pmol/L for fasting insulin and 370.2 pmol/L for postprandial insulin). Furthermore, both predicted fasting and predicted postprandial insulin concentrations were greater for those with the high tertile of abdomen-hip ratio than for those with the low tertile of abdomen-hip ratio.

## Discussion

Of the men followed in the Normative Aging Study, overall adiposity (represented by body mass index) was found to be positively related to both fasting and postprandial serum insulin concentrations. Examination of these data by analysis of covariance and multiple regression showed that serum insulin concentrations increased with increasing body mass index after adjustment for the other covariates. In addition to overall adiposity, the centripetal distribution of body fat (represented by abdomen-hip ratio) was found to be significantly associated with fasting and postprandial serum insulin concentrations, independent of total body adiposity.

When the relationship of diet and insulin was examined, both fasting and postprandial serum insulin increased with increasing saturated fatty acid, after adjustment for total energy. Saturated fatty acid remained a significant predictor of fasting and postprandial insulin concentrations, after further adjustment for total body adiposity and body-fat distribution. These findings were consistent with evidence that the association of saturated fatty acid with insulin was independent of total energy intake. Physical activity was also found to be a significant inverse predictor of postprandial serum insulin concentrations in the multivariate model.

Our findings are consistent with previous studies, which showed a positive association of body mass index and serum insulin concentrations. This association has been demonstrated in both adults (25) and children (26). Other studies have also shown that body-fat distribution (represented by the waist-hip ratio) is associated with insulin resistance and hyperinsulinemia (27, 28). Although both body mass index and body-fat distribution were statistically significantly associated with serum insulin concentration in our investigation, these indexes of obesity are not completely independent ($r = 0.43$; $P < 0.01$). A similar correlation between body mass index and abdomen-hip ratio ($r = 0.52$) was reported in a previous investigation (29). Although these indexes of obesity were correlated, the multivariate model indicated that both body mass index and abdomen-hip ratio were independent predictors of serum insulin concentrations.

Recent reviews have attempted to develop a pathophysiologic model to explain metabolic aberrations (ie, glucose intolerance and hyperlipidemia) and cardiovascular risk associated with abdominal fat (12, 13). The relationship between intraabdominal fat deposition and hyperinsulinemia, however, is not completely understood. Kissebah et al (30) found differences in fat-cell morphology and metabolic activity of adipocytes located in different regions. Intraabdominal adipocytes were found to be larger and more metabolically active than adipocytes located in the gluteal or femoral region. Abdominal adipocytes have also been found to be more responsive to adrenergic agonists; the stimulation of lipolysis in this region is believed to result in a greater release of free fatty acids into the portal circulation. The enhanced release of free fatty acids in splanchnic blood may result in peripheral hyperinsulinemia because free fatty acids have been shown to inhibit extraction of insulin by the liver (31).

The relationships among diet, insulin concentrations, and insulin resistance have been examined in studies of both animals and humans. In two animal studies, Storlien et al (15, 32) demonstrated that the composition of the diet has an important influence on insulin concentrations and insulin resistance. In one of these studies, adult male rats fed a diet high in fat developed insulin resistance (15). The short-term change in the diet from mainly carbohydrates to fat, without a change in body weight

or energy intake, induced insulin resistance. In a metabolic-ward study, Grey and Kipnis (14) examined the effect of dietary composition on hyperinsulinemia in obese humans. To assess the effects of diet on insulin concentrations, subjects were fed an isoenergetic, low-carbohydrate (25%) diet for 3 wk, followed by an isoenergetic, high-carbohydrate (62%) diet for the subsequent 3 wk. Basal insulin concentrations increased with an increase in carbohydrate intake (14). In contrast, no association was found between carbohydrate intake and serum insulin concentrations in the present study.

The differences in results between the Grey and Kipnis study and the present investigation may relate to differences in study design. Grey and Kipnis performed a short-term (3-wk) dietary study on a metabolic ward where diet and total energy intake were completely controlled, whereas our epidemiologic investigation examined self-reported dietary intake over a 1-y period. Their study dealt with the responses of insulin-resistant obese subjects to short-term carbohydrate loading. Our study examined the relationship of long-term macronutrient ingestion to fasting and postprandial insulin concentrations, which are thought to reflect insulin resistance.

Many reports have suggested that the physiologic effects of adiposity are mediated, in part, by insulin (26, 33, 34). However, these analyses examined the relationship of insulin and obesity using only fasting insulin. The present analysis also examined the relationship of saturated fatty acid to postprandial insulin, which may be a more sensitive index of insulin resistance (9). The effects of both saturated fatty acid and body habitus on the increase in insulin concentrations were greater for postprandial insulin than for fasting insulin. These relationships were present despite the greater variability in postprandial insulin values. Greater variability in postprandial values may have been due to measurements being made at one point in time (2 h after the oral glucose-tolerance test). The single time point may, in fact, reflect different points on each individual's insulin curve. Although it is not possible to quantitatively assess insulin resistance precisely in an epidemiologic study, the effect of diet on fasting and postprandial insulin concentrations is compatible with an effect on insulin resistance. Results from the present study lend support to the hypothesis that saturated fatty intake stimulates insulin, which favors the development of large hypertrophic adipocytes distributed in the abdomen and upper-body regions. These adipocytes are sensitive to the antilipolytic effects of insulin and as obesity progresses, insulin resistance develops (10).

Physical activity was also found to be a significant independent predictor of postprandial serum insulin concentrations in the multivariate model. The inverse association of physical activity with serum postprandial insulin is consistent with observations indicating that exercise decreases insulin resistance. Krotkiewski et al (35), for example, demonstrated that repetitive aerobic exercise was associated with a decrease in plasma insulin and an increase in insulin sensitivity, even without a decrease in body weight. This observation in our report supports the usefulness of the exercise questionnaire and provides evidence that the insulin concentrations reported here indeed reflect differences in insulin sensitivity.

A few constraints on the interpretation of these data must be considered. The food-frequency questionnaire used in the present study has been extensively validated (18) and represents the most reasonable means of measuring dietary intake in epidemiologic studies (36). There are, however, potential limitations in using this technique. Data obtained from the food-frequency questionnaire are measured with some error. It has also been suggested that subjects tend to report greater consumption of foods thought to be socially desirable (37). Both of these effects would tend to bias the saturated fatty acid-insulin association toward the null value or no effect. Despite the possible bias, a positive association was noted for both fasting and postprandial serum insulin and saturated fatty acid in the present study. An additional point suggests that our investigation may have underestimated the associations of obesity, body-fat distribution, and saturated fatty acid intake with insulin resistance. We excluded diabetic subjects from the analysis; because these subjects were obese and had elevated abdomen-hip ratios, their exclusion would tend to bias our results toward no effect. Hormonal concentrations may be important in determining body-fat distribution and hence insulin resistance (12). Information on this variable might have improved the precision of our analysis.

The effect of a reduction in dietary saturated fatty acid intake on serum insulin concentration is substantial. A reduction in saturated fatty acids from 20% of total energy to 5% of total energy in an individual in our study population would be associated with a reduction in fasting insulin of 26% and in postprandial insulin of 32%, regardless of the abdomen-hip ratio (Table 3). These results must be interpreted with caution because individuals may not be at equal risk. For example, subjects with a family history of diabetes, information not available to us in this investigation, may be particularly susceptible to the effects of dietary fat on serum insulin concentration. This is not, however, reflected by our model.

The precise public health implications of these findings are unknown because quantitative information on the relationship between insulin and cardiovascular risk is just beginning to emerge. Because hyperinsulinemia and insulin resistance have been linked to hypertension (8), reduction in insulin concentrations may reduce the risk of hypertension and possibly the risk of both stroke and coronary artery disease. In addition, epidemiologic studies have shown that $\approx$80% of individuals with non-insulin-dependent diabetes mellitus (NIDDM) are obese (38). The link between NIDDM and obesity is thought to be insulin resistance. Although the mechanisms for insulin resistance are not completely understood, it has been suggested that aberrations of insulin binding at the receptor site may be involved (39). Results from animal studies suggest that the type of dietary fat consumed may affect the composition of the cell membrane, which in turn may alter insulin-stimulated functions in the cell. Field et al (39) demonstrated that the composition of structural lipids in the adipocyte membrane were altered in rats fed a high-fat diet. The altered membrane composition was also associated with changes in insulin binding. They also demonstrated that the membrane composition, which is altered in diabetic rats, can to some degree be attenuated by dietary treatment. Storlien et al (40) demonstrated that specific fatty acids affect insulin sensitivity. They demonstrated that replacing only 6% of linoleic $\omega$-6 fatty acids with long-chain polyunsaturated $\omega$-3 fatty acids from fish oil prevented the development of insulin resistance in rats. Although these observations cannot be taken as evidence of causal relation, evidence suggests that dietary management may play a role in modulating insulin action within cells. Only prospective studies will determine whether dietary fat intake predicts the development of insulin resistance and NIDDM.

A report by Van Itallie (41) has estimated that 35 million people in the United States are obese (defined as body weight > 20% above the ideal weight). Other conditions associated with upper-body obesity, in addition to NIDDM, include hypertension (42), hypertriglyceridemia, and decreased high-density-lipoprotein cholesterol in women (43), and ischemic heart disease (1). The pathophysiology that explains these associations is not certain although increased insulin secretion and hyperinsulinemia appear to play a central role. The identification of factors related to hyperinsulinemia, such as increased saturated fatty acid intake, obesity, increased centripetal body-fat distribution, and decreased physical activity are potentially important, because they point to testable strategies for risk reduction. These preliminary results suggest the possibility that reduction in saturated fatty acid intake, overall weight reduction, and increased physical activity may diminish the risk of cardiovascular disease and diabetes mellitus by improving insulin sensitivity.

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