

Use and storage of carbohydrate and fat¹⁻³

Jean-Pierre Flatt

ABSTRACT Starch, sugars, and triglycerides provide the bulk of dietary energy. To preserve homeostasis, most of the glucose and fat absorbed must be stored to be mobilized later at rates appropriate to bring about the oxidation of a fuel mix matching on average the macronutrient distribution in the diet. The body's glycogen stores are so small that regulatory mechanisms capable of efficiently adjusting carbohydrate oxidation to carbohydrate intake have developed through evolution. Fat oxidation is regulated primarily by events pertaining to the body's carbohydrate economy, rather than by fat intake. Adjustment of fat oxidation to intake occurs because cumulative errors in the fat balance lead over time to changes in adipose tissue mass, which can substantially alter free fatty acid concentration, insulin sensitivity, and fat oxidation. Fat intake and habitual glycogen concentrations are important in determining how fat one has to be to oxidize as much fat as one eats. *Am J Clin Nutr* 1995;61(suppl):952S–9S.

KEY WORDS Dietary carbohydrate, dietary fat, glycogen, body fat content, weight maintenance, macronutrient balance, respiratory quotient, obesity, exercise

Introduction

Carbohydrates and fats provide most of the dietary energy, and glucose and fatty acids are the main form in which they are distributed throughout the body. These metabolic fuels are used with similar efficiency to regenerate the ATP used by the body's metabolic activities. However, the central nervous system and a few other specialized cells cannot use fatty acids to meet their energy needs, which must therefore be supplied with glucose. The human body adjusts readily to considerable differences in the relative proportions of carbohydrate and fat in the diet, even when major changes in the carbohydrate-to-fat ratio occur (1). Because the fraction of total dietary energy provided by protein is relatively small and relatively constant, and because the body spontaneously maintains a nearly constant protein content by adjusting amino acid oxidation to amino acid intake, body weight maintenance is primarily determined by the intake and utilization of carbohydrate and fat.

The regulation of body weight is a complex problem and many factors are involved in preventing or causing obesity—some are inherited, and others are related to lifestyle and to socioeconomic and dietary variables (2). The aim of this article is to review the main features of carbohydrate and fat metabolism for a better understanding of the roles these macronutrients play in the maintenance of stable body weights and in

influencing the body composition at which weight stabilization tends to occur. Such understanding is important in providing a rational basis for the evaluation of various arguments about the effect of dietary carbohydrate and fat on body weight regulation.

Carbohydrate storage

The most abundant forms of edible carbohydrates are the starches provided by grains and tubers. They provide the bulk of human energy needs, except in affluent Western societies where fat is a major source of energy and where sucrose supplies almost as much energy as starch (3). It is helpful to understand the particular problem that the organism has to solve when processing carbohydrates. For carbohydrates to be absorbed, they must first be broken down into monosaccharides. Small molecules exert a powerful osmotic effect and it is therefore important that intestinal absorption be able to keep up with the rate of starch hydrolysis. Furthermore, absorption must be completed before carbohydrates are subjected to bacterial fermentation; otherwise, there are unpleasant side effects, such as those experienced after lactose ingestion by individuals with low intestinal lactase activity. Meals commonly supply 50–150 g carbohydrate. This is much more than the 15–25 g free glucose present in the body, of which only 5 g is in the blood itself. To avoid hyperglycemia and spillage of glucose into the urine, glucose transferred into the circulation must be rapidly transferred into cells. Because glucose oxidation in the postprandial state consumes only ≈ 10 g/h, most of the glucose taken up must be stored by conversion to glycogen, primarily in liver and muscle. Glucose uptake and glycogen synthesis are greatly stimulated by insulin, the secretion of which increases when blood glucose concentrations rise (4). Two moles ATP are expended to incorporate 1 mol glucose into glycogen. Because 36 ATP are gained during the complete oxidation of one molecule of glucose, 2/36, or $\approx 5\%$ of the energy content of glucose must be expended to store it as glycogen.

Glycogen molecules are very large; they are thus effectively trapped in the cells in which they were made without creating much of an osmotic effect. In view of the hydrophilic nature of carbohydrates, glycogen is associated with ≈ 3 g water/g glycogen. The energy density of glycogen stores is thus only

¹ From the University of Massachusetts Medical School, Worcester, MA.

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³ Address reprint requests to J-P Flatt, Department of Biochemistry, University of Massachusetts Medical Center, Worcester, MA 01655.

≈ 4.2 kJ/g (≈ 1 kcal/g), imposing definite limits on the amount of energy that can conveniently be carried in the form of glycogen. Glycogen concentrations are highest in the liver, ie, typically $\approx 4\%$ after an overnight fast, and up to 8% after meals (5). Because an adult's liver weighs ≈ 1.5 kg, hepatic glycogen storage capacity is limited to ≈ 120 g. Glycogen amounts in muscle are much lower and deliberate carbohydrate loading is necessary to raise them much above 2% (5). However, because muscle accounts for 20–30% of total body weight, the amount of glycogen stored in muscle is generally three to four times that in the liver. Total glycogen stores in adults can thus be estimated to be ≈ 200 – 500 g, depending on body size and on the amount of carbohydrate consumed, and vary substantially during the day as a function of food intake and exertion. The body's glycogen reserve is in effect not much greater than the amount of carbohydrate usually consumed in 1 d, and maintenance of glycogen amounts within a desirable range requires effective adjustment of carbohydrate oxidation to carbohydrate intake.

Marked glycogen depletion causes a threat to the ability of the liver to ensure adequate circulating blood glucose concentrations, which requires the release of ≥ 5 g glucose/h (or ≈ 100 mg/min) to replace the glucose removed by the nervous system. Because the influx of nutrients from the intestine occurs through the portal system, the liver has a prime opportunity to replenish its glycogen reserve after consumption of carbohydrates. Usually, this demands only a fraction of the carbohydrates provided by a meal and substantial amounts of glucose reach the periphery and are stored in muscle. The relative roles of liver and muscle in the disposition of a carbohydrate load vary depending on the degree of depletion of the glycogen stores, the size of the meal, and the type of carbohydrate consumed (6–8). It seems reasonable to envision that after a typical meal one-quarter to one-third of the carbohydrate is converted to glycogen in the liver and one-third to one-half to glycogen in muscle, whereas the remainder is oxidized during the postprandial hours.

Fat storage

The oils and fats accumulated by plants and animals are triglycerides containing three fatty acids molecules esterified to one molecule of glycerol. The glycerol accounts for $\approx 10\%$ of the weight of long-chain triglycerides (or 5% of their energy content), providing a small but critical amount of glucogenic precursors during periods of starvation (or severe carbohydrate deprivation) (4). Because of their insolubility in water, triglycerides do not influence substrate concentrations in the body's aqueous compartments, remaining metabolically unnoticed whether present in small or large amounts, and fats can be stored without bound water. In the fat cells that make up adipose tissue, triglycerides form a central fat droplet (much larger by itself than most of the body's other cells) that is surrounded by a thin layer of metabolically active cytoplasm. These adipocytes can expand or shrink considerably, but once formed, their number cannot be reduced by fasting, only their size (9). A delicate network of capillary blood vessels and nerve terminals permeates the body's adipose tissue, $\approx 85\%$ of which is fat. This allows ≈ 33.5 kJ (8 kcal) energy to be stored per gram

of tissue, making it possible for animals to accumulate and carry a reserve of fuel substantial enough to allow survival during extended periods of food deprivation (4).

Dietary fats are emulsified in the intestine with the help of bile and then degraded to fatty acids and glucose by pancreatic and intestinal lipases. These are absorbed from the lumen, reesterified into triglycerides by the intestinal cells, and secreted into the lymphatic vessels, draining the mesentery in the form of chylomicrons. These tiny lipid droplets are solubilized by a thin coating of lipoproteins, allowing them to remain in the circulation. They give the plasma its milky appearance a few hours after a fatty meal has been consumed. To be transferred into cells, the triglycerides of the chylomicrons must be hydrolyzed, a function carried out by lipoprotein lipase (LPL), an enzyme produced most abundantly by the endothelial cells of adipose tissue capillaries. The fatty acids produced by LPL are promptly taken up by the fat cells and reesterified, only a small fraction escaping to reach the pool of albumin-bound fatty acids (10), the form in which fatty acids are made available as a metabolic fuel. Dietary fatty acids are thus targeted for deposition in adipose tissue.

Conversion of carbohydrate into fat

Conversion of carbohydrate into fat allows animals to build up fat reserves even when their feed contains very little fat. In adult humans such *de novo* lipogenesis is primarily a hepatic process (5). Quantitatively, this conversion plays an insignificant role in adults consuming mixed diets (11). Even after ingestion of 500 g carbohydrate, the nonprotein respiratory quotient (RQ) (ie, the ratio of CO_2 produced to O_2 consumed by carbohydrate and fat metabolism) does not rise above 1.0, which indicates that fatty acids are being synthesized at a rate exceeding the concomitant rate of fat oxidation (Figure 1) (12). Thus, unusually large, occasional carbohydrate loads are handled primarily by converting the absorbed glucose into glycogen. The massive expansion of the glycogen stores then leads to the nearly exclusive use of glucose as a fuel (as shown in Figure 1 by the fact that the RQ remains close to 1.0 for many hours), in time reducing such temporary accumulations of glycogen. To induce substantial rates of carbohydrate conversion into fat, the body's total glycogen stores must be considerably raised, from their usual 4–6 g/kg body wt to > 8 – 10 g/kg body wt. This requires deliberate and sustained overconsumption of large amounts of carbohydrates for ≥ 2 – 3 d (13).

Two important conclusions can be deduced from these observations: 1) under usual conditions of unrestricted access to food, glycogen stores are spontaneously maintained far below their maximal capacity, and 2) the common belief that carbohydrates are readily turned into fat can be dismissed as well as the frequently made argument that the high metabolic cost of lipogenesis is a cause for greater energy dissipation on high-carbohydrate diets. It should not be overlooked, however, that consumption of carbohydrates reduces the need to use fat as a fuel, so that carbohydrate intake is an important factor in determining how much of the fat consumed will be retained.

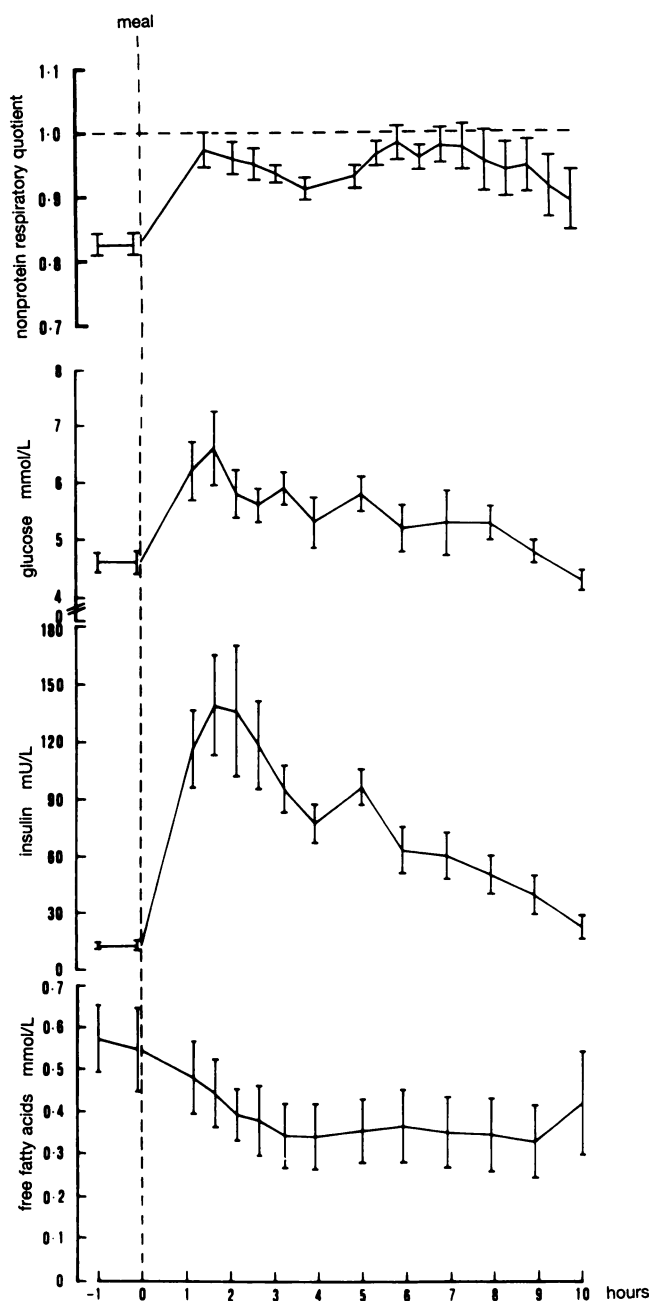


FIGURE 1. Changes in the nonprotein respiratory quotient, in blood glucose, and in plasma insulin and free fatty acid concentrations observed in six young men in response to a breakfast providing 8372 kJ (2000 kcal) carbohydrate (white bread, jam, and fruit juice). $\bar{x} \pm \text{SEM}$. Reproduced with permission (12).

Carbohydrate oxidation and regulation of the carbohydrate balance

Because glucose is constantly used and its availability is critical, regulatory mechanisms evolved that are able to effectively prevent hypoglycemia. Declining blood glucose concentrations thus elicit the release of glucagon, which accelerates the rate of glucose release by the liver by activating phosphorylase to degrade glycogen, as well as by enhancing

gluconeogenesis from amino acid and lactate (6, 7). Insulin, which in the postprandial state acts to prevent hyperglycemia by promoting glucose uptake and its conversion into glycogen, also provides a signal to restrain hepatic glucose release when blood glucose concentrations are sufficiently high (4). Phosphorylase in muscle is activated by catecholamines, primarily during muscle contraction to make glucose available locally to permit rapid ATP resynthesis by anaerobic glycolysis as well as by oxidation of glucose.

To ensure the body's ability to maintain glycogen reserves that can sufficiently sustain adequate blood glucose concentrations at all times, mechanisms developed through evolution that restrict glucose oxidation whenever food intake fails to replenish the glycogen reserve. Yet glucose must also be allowed to be the major metabolic fuel because foods often provide most of their energy in the form of carbohydrates. As shown by a rapid rise in the RQ after carbohydrate ingestion (Figure 1), the contribution made by glucose to the fuel mix oxidized indeed increases rapidly after carbohydrate intake. Because hypoglycemia rarely occurs and glucosuria is effectively avoided under widely differing nutritional and metabolic conditions, it is evident that these mechanisms operate effectively in adjusting the rates of glucose storage, mobilization, and oxidation and in maintaining glycogen amounts in an appropriate range.

Maintenance of stable glycogen amounts when there is free access to food would be greatly facilitated if adjustment of glucose oxidation to carbohydrate intake were complemented by signals working to diminish or enhance food intake when glucose concentrations and/or glycogen reserves rise or decline excessively (14). This type of regulation appears to operate in modulating changes in food intake from day to day in mice fed *ad libitum* (15, 16), but attempts to demonstrate a similar behavior in humans have so far been unsuccessful (1). What is known for humans is that hypoglycemia induces an extremely powerful urge to find food, that food intake in free-living individuals is such that glycogen stores are maintained well below their maximal capacity, and that increases (or decreases) in the diet's carbohydrate content lead to decreases (or increases) in energy intake (17–19).

Fat oxidation and fat balance

Fat oxidation is determined primarily by the gap between total energy expenditure and the amount of energy ingested in the form of carbohydrate and protein, rather than by the amount of fat consumed on a given day (20). This may seem surprising at first, but it is the consequence of the facts that overall substrate oxidation is determined by body size and physical activity, that amino acid and glucose oxidation rates adjust themselves to the amounts consumed, and that fat oxidation rates can readily be set by indexes unrelated to the body's fat economy because the body's fat reserves are very large. Fat intake, on the other hand, is a function of the fat content of the foods selected and of the amounts of foods consumed, and it is not likely to be influenced by short-term gains or losses of fat (21), which are trivial compared with the body's large fat stores.

The lack of direct regulatory interactions between fat oxidation and fat intake is demonstrated by the changes in fuel

utilization induced by food ingestion. Fats are usually consumed together with carbohydrates. The latter's influence in stimulating insulin secretion leads to an increase in carbohydrate, but a decrease in fat, oxidation. As shown by the experiment described in **Figure 2**, the insulin response and the changes in glucose and fatty acid concentrations induced by eating a breakfast providing 75 g carbohydrate are hardly affected by the addition of 40 g fat as margarine, and the postprandial use of metabolic fuels described by the evolution of the RQ as a function of time is essentially unaffected as well (22). The effect of an 80-g fat supplement is manifest, however, because with such a dose fat ingestion markedly delays and attenuates (but does not prevent) the carbohydrate-induced postprandial rise in the RQ, resulting in an increase of 10 g in fat oxidations, and a decrease of 20 g in glucose oxidation during the 6 h after the meal (10). That fat ingestion has so little effect on postprandial substrate oxidation is imputable to the relatively slow rate of fat absorption from the gut and to the fact that dietary fat is converted into chylomicrons targeted for deposition in adipocytes, allowing only a small fraction to reach other cells in the form of free fatty acids (10). Thus, although carbohydrate intake has a powerful effect in promoting carbohydrate oxidation, ingestion of fat promotes fat oxidation only marginally, so that even the consumption of high-fat meals leads to inhibition of fat oxidation during the following hours. On days with high food intake, during which carbohydrate oxidation is increased to limit excessive glycogen accumulation, fat oxidation is curtailed, compounding fat gains (15, 16). Furthermore, because carbohydrate and protein balances hover around zero, errors made in maintaining fat balance are the main determinant of the overall energy balance (23)—and the energy balance cannot be expected to be regulated more accurately than the poorly regulated fat balance (24).

If fat balance is maintained far less accurately than carbohydrate (and protein) balances, how is it that most individuals, even though they eat food mixtures with different fat contents, tend to maintain a relatively stable body composition (which implies that adjustment of fat oxidation to fat intake does occur, at least in the long run)? Some increase in fat oxidation with high-fat diets is due to a reduced postprandial inhibition of fat oxidation when fat-containing meals are consumed, which is a consequence of the fact that fat delays gastric emptying and intestinal absorption (10). Because the presence of fat in the foods consumed also results in a lesser intake of carbohydrates, fat-containing meals are followed by lower postprandial insulin release and less inhibition of fat oxidation. With lower carbohydrate intakes, glycogen amounts are likely to be maintained in a lower range, resulting in lower insulin concentrations but higher rates of fatty acid release and oxidation between meals. These effects are indirect, because they are controlled by insulin and mainly serve to regulate carbohydrate metabolism rather than fat metabolism. These phenomena cannot, therefore, be expected to produce an exact compensation.

Whereas short-term errors in the fat balance are too small to affect the size of the body's fat stores, fatty acid concentrations, fat oxidation or food intake, the cumulative effect of repeated imbalances between fat intake and oxidation can in time lead to substantial changes in the size of the adipose tissue. Expansion of the fat mass, whether as the result of an increase in the number of fat cells and/or an enlargement of the adipocytes,

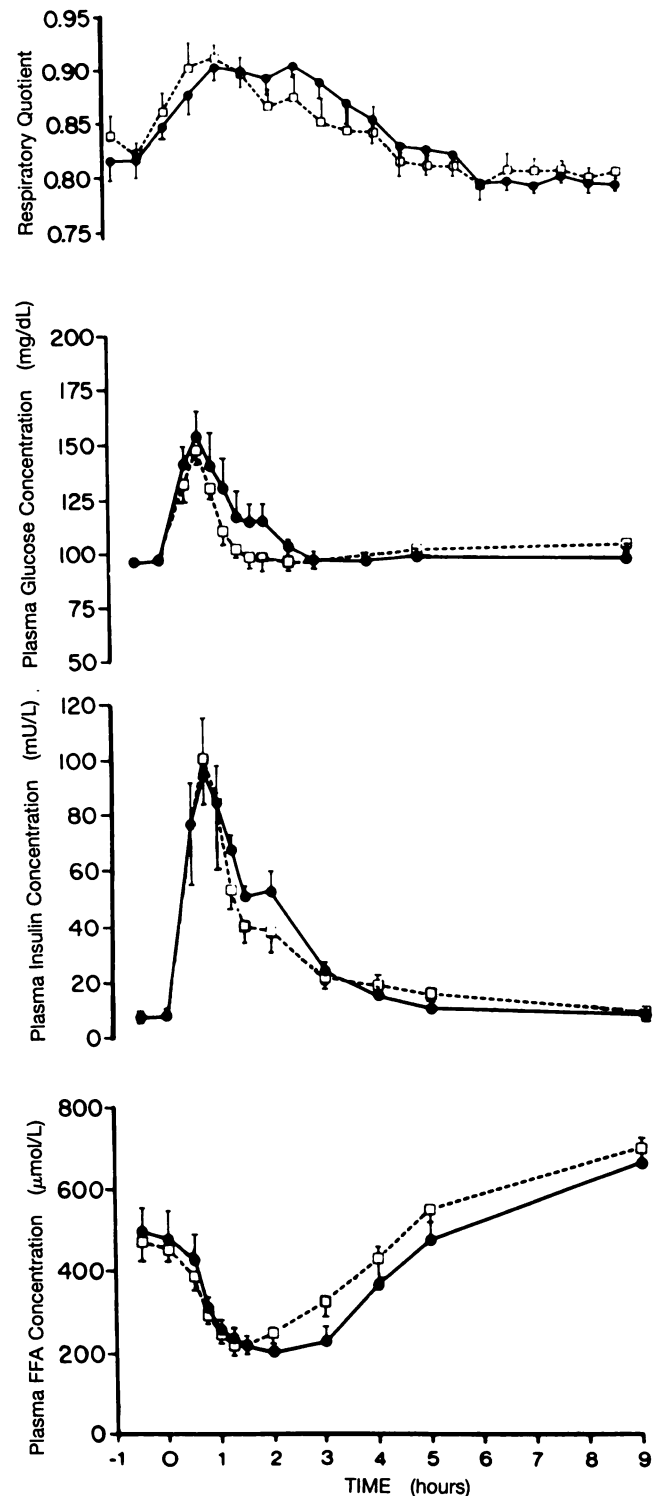


FIGURE 2. Changes in the nonprotein respiratory quotient, in blood glucose, and in plasma insulin and free fatty acid concentrations observed in seven young men in response to a low-fat breakfast of white bread, jam, and dried meat (73 g carbohydrate, 6 g fat, and 30 g protein, ●—●), and after consuming the same breakfast on another day with a supplement of 50 g margarine (41 g additional fat, □—□). $\bar{x} \pm \text{SEM}$. For plasma glucose, $\text{mg/dL} \times 0.05551 = \text{mmol/L}$. Adapted from reference 22 with permission.

causes an increase in fatty acid release, which leads to higher free fatty acid concentrations (25) and to a type of insulin resistance susceptible to enhancing fat oxidation relative to glucose oxidation (15, 26, 27). Enlargement of the fat masses thus promotes fat oxidation, just as well-filled glycogen stores promote glucose oxidation. Furthermore, it is evident that the effect of abdominal fat accumulation on fatty acid concentrations and intermediary metabolism is greater than that of peripheral fat deposition (28). However, whereas carbohydrate intake promptly alters the contribution made by glucose to the fuel mix oxidized, the increase in fat oxidation brought about by expansion of the adipose tissue mass is chronic, rather than related to recent fat intake (29). Through this chronic effect, a particular body composition will in time be reached (or approached) for which the oxidation of fat makes a contribution to total fuel oxidation that is commensurate, on average, with the diet's fat content. A steady state is then reached where not only the body's glycogen reserves and protein pools, but also its fat content, tend to remain constant (15, 30).

Changes in glycogen concentrations do not affect body weight noticeably, but the changes in body fat content needed to alter the contribution made by fatty acids to the fuel mix oxidized can markedly affect body weight. Thus, the problem of body weight regulation can, in effect, be focused on the issue: How fat does one have to be to oxidize as much fat as one eats?

Factors affecting body fat content

Dietary fat content

It is well established that diets with high fat contents tend to increase the incidence of obesity in most experimental animal models, although the extent of this response varies (31). In mice given free access to one of a series of diets containing different proportions of fat and carbohydrate, the weight maintenance plateau is reached at increasingly higher degrees of adiposity as the proportion of dietary energy from fat increases from 15% to 60% (Figure 3) (15, 16). When access to food is unrestricted, spontaneous reductions in glycogen amounts are not enough to allow an increase in fat oxidation that is sufficient to prevent increments in the diet's fat content from leading to fat accumulation. Thus, weight maintenance with high-fat diets becomes established for higher degrees of adiposity (15, 30). Figure 3 shows that over the range of fat contents typical of the mixed diets consumed in affluent societies, there is a dose-response relationship between carcass fat content and dietary fat content. This is consistent with the widely held view that the relatively high fat content of mixed diets is an important factor in explaining the high incidence of obesity in affluent societies (3, 31–33). The apparent aberration in the dose-response curve when dietary fat is very low is due to the active rate of lipogenesis that such diets induce in small animals. Note also that the range of interindividual variations in fatness becomes wider with high-fat diets, even in highly inbred mice (lower panel of Figure 3). This suggests that even minor individual differences can lead to substantial variability in the size of the adipose tissue mass, and, as a corollary, that changes in adipose tissue mass have a rather weak effect on metabolism and hence are well tolerated. This provides a simple explanation for a puzzling aspect of the obesity

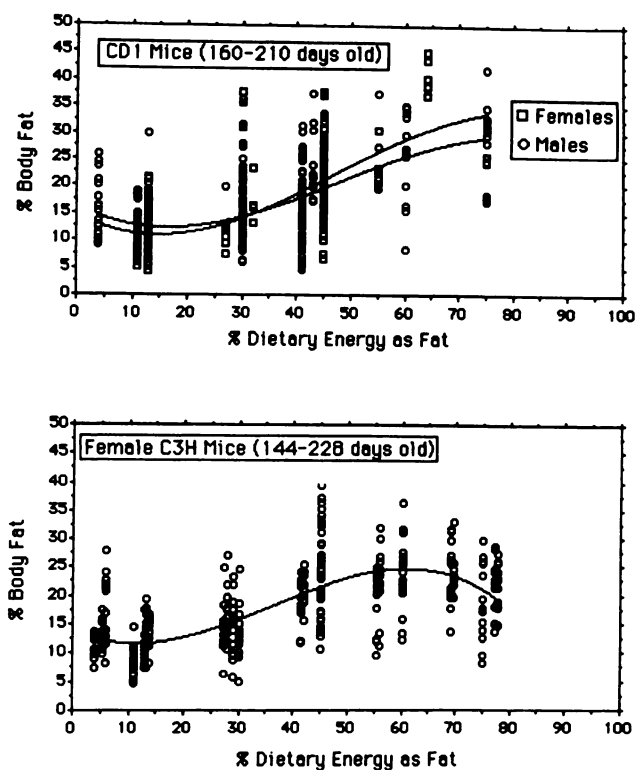


FIGURE 3. Body fat content determined by carcass analysis in mice maintained on ad libitum diets containing the fraction of total energy shown on the abscissa in the form of fat, 18% as protein, and the balance as carbohydrate (half as starch and half as sucrose). Upper panel: male (○) or female (□) CD1 mice; lower panel: female C3H mice. Reproduced with permission (32).

problem, namely the great diversity in body fatness encountered in affluent populations. It may also account for the fact that the positive correlations between dietary fat content and the degree of adiposity documented in humans are relatively weak in epidemiological studies (34–37).

Effect of habitual glycogen concentrations

Total energy intake in animals fed ad libitum increases when they are provided with sugar or polyose solutions in addition to solid food, although consumption of solid food is reduced (38). Increased fat accumulation occurs despite a lesser fat intake, because the increased influx of carbohydrate raises insulin and glycogen concentrations, thereby curtailing fatty acid oxidation and inducing lipogenesis. As shown by comparing Figures 1 and 2, the amount of carbohydrate consumed and its effect on raising the body's glycogen stores influences postprandial and postabsorptive RQs. The degree of replenishment of the glycogen stores is thus an important factor in determining the contribution made by glucose, and hence by fat, to the fuel mixture oxidized. When glycogen reserves are kept in an elevated range, a greater expansion of the adipose tissue mass is necessary to make fat oxidation commensurate with fat intake. Multiple-regression analysis of the data shown in the upper panel of Figure 3 shows that body fat is higher in the mice that had relatively high liver glycogen concentrations at the time of sacrifice, ie:

% Body fat

$$= 5.7 + 0.24 (\pm 0.02)$$

× % dietary fat

$$+ 0.95 (\pm 0.20)$$

× % liver glycogen

(\pm indicates SE; $n = 400$; $R^2 = 0.33$; $P < 0.0001$).

Effect of food variety and palatability

Provision of a selection of highly palatable foods (supermarket or cafeteria diets) to experimental animals causes them to overeat markedly (31, 39). However, even under conditions of unrestricted access, food intake diminishes spontaneously after weight gain (40). Expansion of the adipose tissue mass, which may or may not be complemented by changes in glycogen concentrations, can therefore compensate for differences in food palatability, permitting the steady state of weight maintenance to become reestablished, but at a higher degree of adiposity.

The diets consumed in affluent societies are commonly referred to as mixed diets because they provide macronutrient mixtures in which carbohydrates, fats, and protein all contribute substantial amounts of energy. This not only endows them with a relatively high fat content, but also allows for a remarkably wide diversity of highly appetizing food items. Food availability, palatability, and variety can be expected to influence food intake in humans as well as in animals (41). A varied selection of appealing dishes enhances meal size, because satiety mechanisms must reach greater intensity to restrict further food intake than when faced with unappealing foods (42). This tends to raise the upper limit of the range within which glycogen concentrations are habitually maintained. In addition, the ubiquitous availability of foods, by inducing eating between meals, can have the effect of keeping glycogen concentrations high. Given the ensuing curtailment of fat oxidation, fat will accumulate until expansion of the adipose tissue mass is sufficient to bring about a rate of fat oxidation commensurate with fat intake, permitting the steady state of weight maintenance to become established. There is much room for this effect if one considers that the range within which glycogen is maintained is not precisely determined because glycogen reserves are maintained far below their level of saturation even under conditions of unrestricted access to food (12, 13). The influence of the palatability, variety, and accessibility characteristics of the food supply on habitual glycogen concentrations, and hence on fat oxidation, need to be taken into consideration when accounting for the high incidence of obesity in affluent societies, as well as when setting up conditions to facilitate weight control.

Effect of physical activity

The habit of engaging in substantial physical activities is generally quite effective in limiting the accumulation of excess weight, or in inducing loss of excess adipose tissue (43). Yet it is generally not well understood why increments in food intake elicited by exercise are sometimes sufficient to ensure weight maintenance (ie, in a physically active individual), but sometimes not (ie, when someone initiates a physical training pro-

gram). In mice fed ad libitum, spontaneous running activity causes a decrease in the average daily RQ, indicating that physical activity promotes fat oxidation to a greater extent than it does carbohydrate oxidation (15, 16, 44). This is not surprising, because exercise elicits great increases in substrate oxidation in muscle, which uses fatty acids as well as glucose. In addition, the exercise-induced depletion of the glycogen reserves can lead to lower RQs not only during the exercise but also during the postexercise periods of the day (44, 45). When substantial physical activity is part of the daily routine, the steady state of weight maintenance is reached with a lesser expansion of the adipose tissue mass.

Macronutrient selection and weight control

Weight maintenance requires that the body's metabolism oxidize as much glucose, fatty acids, and amino acids as are supplied by the diet. The goal is to achieve this steady state without the need for an undesirable expansion of the adipose tissue mass (46). This goal is more readily achieved when a diet with a high carbohydrate content is consumed because it is obviously easier to burn as much fat as one eats when one does not eat a lot of fat. Exercise provides additional leverage because it causes a greater increase in the oxidation of fat than of glucose.

Because the body will spontaneously and effectively maintain protein and carbohydrate balances, but does not (or cannot) regulate the fat balance nearly as accurately (14–24), it makes sense to direct voluntary efforts at this relatively soft target. Furthermore, concentrating on the fat balance provides a more specific goal than one based on overall energy exchanges. Awareness of the fact that fatty foods have a particularly high energy density, and that low-fat diets provide more bulk, led dietitians long ago to recommend low-fat diets for weight control (47). Recommendations to reduce fat intake have indeed been increasingly promulgated in dietary guidelines published by government agencies and medical or health-related associations, because limiting fat intake (particularly the consumption of saturated fats) appears to be a key measure in lowering blood cholesterol concentrations and in minimizing the development of arteriosclerosis (48, 49). To these reasons for restricting fat intake one can add the further argument that the steady state of weight maintenance can be expected, for metabolic fuel balance reasons, to be achieved with smaller adipose tissue stores when the diet's fat content is low.


In the consideration of the advantages of relying on high-carbohydrate foods to satisfy hunger, a word of caution should be included about the possible disadvantage inherent to rapidly absorbed carbohydrates. It is now known that a slight temporary decline in blood glucose concentrations is a physiological event that can lead to initiation of food intake (50, 51). In animals consuming a feed of fixed composition, the time elapsed when this event occurs is proportional to the size of the preceding meal (50). It may well be linked to the end of carbohydrate influx from the gut, when the liver has to shift from a glucose-removing state to a glucose-releasing state. Rapidly absorbed carbohydrates would be expected to cause this signal to occur not only earlier, but also more sharply, in view of the high degree of postprandial insulinization that they elicit and the rapid rates of peripheral glucose utilization in-

duced by high insulin concentrations. One would therefore anticipate that complex carbohydrates (eg, whole-grain products in which starch is still associated with natural fiber, undercooked starch, and vegetables), which are absorbed more slowly, have a low glycemic index, and are less insulinogenic (52), would be less likely to trigger a signal that may lead to early food consumption and therefore would exert a more prolonged satiating influence (47).

Dietary carbohydrates also differ by the extent to which they inhibit postprandial fat oxidation and affect the proportions of glycogen deposited in liver or muscle. Recognizing that the critical issue for weight control is the difficulty of oxidizing as much fat as one eats, it would seem advantageous to avoid the carbohydrates that most inhibit fat oxidation postprandially, and perhaps those that most raise hepatic glycogen stores. Such a selection can be based in part on their glycemic index (53), although not entirely; for example, fructose is not insulinogenic and does not raise glucose concentrations but markedly raises the RQ (54, 55) and favors the build-up of liver glycogen (8).

The arguments reviewed here suggest that a reduction in fat intake, if substantial, may represent a long-term measure capable of reducing the need for an expanded adipose tissue mass in achieving the steady state of spontaneous weight maintenance. This expectation is supported by the weight loss experienced by subjects to whom a line of low-fat foods, designed to be of comparable palatability with control foods of typical fat contents, was offered ad libitum (17, 18), and subjects who were coached in avoiding fatty foods while eating to satiety (56). Restricting fat intake also appears to be a crucial dietary measure in helping to limit and delay weight regain after periods of dieting because fat accumulation occurs by storage of dietary fatty acids, rather than by conversion of carbohydrate into fatty acids (11–13). The admonition to restrict fat intake but to eat carbohydrate freely may be reasonable for individuals aiming to maintain weight, but it is probably counterproductive in promoting weight loss because it will attenuate the impact of a reduction in fat intake on the energy balance. For effective weight reduction, a reduction in fat intake should be complemented by efforts to limit (at least to the extent of not increasing) carbohydrate intake, to reduce sugar intake, and to select foods high in complex carbohydrates.

There is not enough information to judge to what extent fat intake has to be reduced to prevent obesity and this limit is in fact likely to vary for different individuals. It seems unlikely that meeting the 30% target proposed by current guidelines (48, 49) will by itself be sufficient to prevent excess weight in individuals prone to obesity. However, this measure may have some effect because a cap on fat intake could alter dietary habits in obese subjects, who often have a predilection for fatty foods (33). Note that in calculating the relative proportions of carbohydrate and fat in the diet, energy consumed in the form of alcohol should be included with that provided by fat, because ethanol reduces fat but not carbohydrate oxidation (57). It is of course feasible to reduce fat to 25% or even 20% of total energy intake. Selecting foods with a lower fat, but higher complex carbohydrate content does not so much entail the discomfort of hunger, as it does require the avoidance of a whole range of desirable foods. If done consistently, this practice has the effect of limiting the range of permissible foods. In addition to the metabolic leverage and to the reduction in the

energy density of the allowed foods, this could have another potentially quite significant advantage, namely to facilitate weight control by reducing the diversity of the food assortment from which one can partake. This advantage is perhaps being eroded by the rapid increase in the number of low-fat foods that are now available. 

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