Issues and Misconceptions About Obesity

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Energy is a concept of universal importance. In relation to body weight regulation, one is so used to consider energy intake, energy expenditure, and energy balance that one forgets that energy is an abstract notion without physiological equivalent. The body's regulatory functions may strive to maintain carbohydrate (CHO), protein and/or fat balances, but not energy balance. The body ignores that 1 g of fat contains more than twice the energy present in 1 g of carbohydrate, an element of information needed to determine the energy balance. In applying this knowledge to consider body weight regulation, one introduces a biologically irrelevant fact. One may learn to be in awe at the body's ability to maintain approximate energy balances over extended periods of an individual's life, as a consequence of the organism's ability to maintain substrate balances, but attempts to understand this as the result of a regulatory process directed at the energy balance itself are doomed to be frustrated. Not surprisingly, failure to be aware of the inappropriate use of the energy and energy balance concepts in considering body weight regulation and obesity has spawned numerous misconceptions (1).

The intent of this article is to provide direct access to the considerations that pertain to particular notions commonly cited in the context of obesity. Their presentation under separate headings should be helpful, in particular to individuals not necessarily immersed in obesity research who want to understand the meaning of specific terms and concepts.

1. Problems in applying the energy balance concept

The energy balance equation is often invoked to frame issues relating to body weight regulation and obesity. The equation states that

\[ \text{Energy Balance} = \text{Energy Intake} - \text{Energy Expenditure} \]

which appears to support the statement that obesity is due to a "positive energy balance," i.e., that energy intake is exceeding energy expenditure. Unfortunately, this seemingly obvious pronouncement sets up several misconceptions (1). First, this view confuses past and present, obscuring the fact that obese individuals, like lean subjects, tend to reach a state of approximate energy balance, with similar short-term fluctuations in the energy balance. Thus, one fails to recognize that the really important difference between lean and obese individuals is the degree of adiposity at which, on average, their energy intake tends to adjust itself to their energy expenditure. This varies widely between individuals, in a manner influenced by genetic as well as by environmental conditions. Thus obesity is brought about by a failure of the interactions between body composition and food intake regulation to restrain eating when the body's energy stores are more than adequate for health (Table 1).

2. Problems with the metabolic efficiency concept

Weight gains or losses generally do not exceed 1 or 2 kg per year during long periods of an individual's life (2), reflecting an error of only 1–2% in the adjustment of food intake to energy expenditure. This corresponds to an average daily difference between energy intake and expenditure in the order of 25–50 kcal. Thus even minor differences between energy intake and expenditure appear to be able, in their cumulative long-term effect, to cause or to prevent the progressive development of obesity. The second misconception promoted by notions based on the energy balance equation is that obesity could therefore be due to unusually low metabolic rates. This impression has been enhanced because rates of energy expenditures per kg body weight or per kg fat-free mass (FFM) appear to be lower in obese than in lean subjects, which is a simple artefact due to a positive intercept in the correlations between energy expenditure and body weight.
or FFM. Nevertheless it has led to speculations about higher "metabolic efficiency" in obesity, as a way to account for a higher than normal proportion of energy retention. Such a notion, sometimes tossed around without proper definition of "metabolic efficiency" (3), should long ago have been dispelled by the realization that total energy expenditure is raised in obesity, due to the increase in lean body mass associated with weight gain and the greater costs associated with moving a heavier body. The utter confusion introduced by the energy efficiency concept becomes apparent when one realizes that the large daily variations in food consumption that occur when food is freely available cause energy balance to be positive on some days and negative on others. Thus, during period of weight stability, metabolic efficiency would oscillate between positive and negative values over the short term, whereas it is essentially equal to zero over extended periods.

3. The misleading emphasis on the importance of low resting metabolic rates
Arguments about the potential long-term impact on body weights of differences in resting energy expenditure, or of small diet- or physical activity–induced increases in energy expenditure, hinge on the assumption that such differences would not be offset by adjustments in energy intake. This is a totally unwarranted assumption, as there is no evidence indicating that average energy intakes in subjects eating at their own discretion are "clamped" at some particular level (4).

Several facts speak against the notion that minor differences in metabolic efficiency or in resting energy expenditure may be important for body weight regulation. (i) Stature, which is positively correlated with resting and with total energy expenditures, has no impact on adiposity (5). (ii) There is no correlation between % body fat and deviations from predicted (or "normal") basal energy expenditure (Figure 1) (6).

It is generally considered that causes cannot safely be inferred from correlations, especially from cross-sectional correlations. In the case considered here, however, the crucial fact is the lack of correlation. This is much simpler to interpret, as this evidence directly and simply demonstrates that factors other than deviations from predicted resting metabolic rate are overwhelming the possible effect of such deviations in determining the
degree of adiposity associated with the steady state of weight maintenance.

Various arguments have been made about the potential roles of futile cycles (3) and of brown adipose tissue and uncoupling proteins (UCP) in affecting adiposity by raising energy expenditure (7). However, their impact on overall energy expenditure in man appears to be small at best. Since differences in basal energy expenditure have no statistically recognizable impact on body fat contents, speculations about the potential significance of UCP and futile cycles need to be made cautiously. Given that long-term CHO balance will be maintained under all circumstances, one should only expect an effect on body fat if the resulting increases in energy expenditure were largely covered by increments in fat oxidation, setting up an effect similar to that of physical activity (see #18 below).

At any rate, it is of interest to note that spontaneous food intake regulation is powerful enough to obliterate the impact that meals and foods served in uniform proportions could be expected to exert on fitness among individuals whose energy expenditures differ, for example, due to differences in stature (5).

4. Misleading expectations about the importance of "adaptive thermogenesis"

Adaptive thermogenesis describes changes in resting energy expenditure which serve, or have the effect of diminishing weight gains or weight losses during periods of overconsumption or starvation, relative to the weight changes which would be expected if changes in resting energy expenditure were solely due to changes in body size and in the thermic effect of food (8). This phenomenon has thus been considered to reflect a kind of "metabolic adaptation." While adaptive thermogenesis has been found to be substantial in some animal models, they are modest in humans, to the point that it has been difficult to establish them unambiguously. The fact that differences in resting energy expenditure have no statistically recognizable impact on adiposity (see Figure 1) argues strongly against the view that differences in adaptive thermogenesis, which occur only occasionally, play a significant role in preventing or promoting the preponderance of obesity.

5. Problem in judging the importance of de novo lipogenesis and of its metabolic costs

Several reactions in the fatty acid synthesizing pathway require adenosine triphosphate (ATP), so conversion of glucose into fat requires a substantial investment of energy. If the costs for prior conversion of glucose into glycogen as well as for the transport of fatty acid synthesized in the liver to adipose tissue are also included, the cost for conversion of dietary carbohydrate into fat may be assessed at some 25% (9). The net ATP yield, i.e., the total number of ATP generated minus the number of ATP expended for the transport, activation, and remodeling in the metabolic process, was evaluated in refs. 3 and 10. This yield is higher during fatty acid oxidation than during glucose oxidation. The net
ATP yield from ingested glucose followed by the oxidation of that amount of fat is thus not much affected by initial conversion of glucose to fat, or by the concomitant occurrence of lipogenesis and oxidation of a matching amount of fat (10). Thus, contrary to a still commonly held expectation, dissipation of dietary energy by conversion of glucose into fat cannot explain why high-carbohydrate diets are less conducive to obesity than high-fat diets (11). In fact, the issue is essentially moot, mainly because fatty acid synthesis from glucose, estimated at some 10 g/day (12) in subjects consuming a Western diet, is of minor quantitative significance and not sufficient to compensate for concomitant fat oxidation even after massive CHO loads (13).

6. The irrelevance of the "nutrient-partitioning" concept
The concept of nutrient partitioning has been developed in the context of meat production, where the proportions of nutrients consumed retained as muscle or fat is important. It is relevant for periods of rapid growth, but it has also been considered in discussing the problem of obesity, in attempts to understand the differences in degrees of adiposity reached by different individuals (14). However, in lean as well as in overweight adults whose weight is relatively stable, essentially all the nutrients consumed over a period of a few days are oxidized, regardless of diet, level of physical activity, and degree of adiposity. Furthermore, the large variations in physical activity, food consumption, and energy balance occurring under free-living conditions cause nutrient balances to vary considerably from day to day. Thus the nutrient-partitioning concept is rather meaningless when applied to adult humans.

7. Failure to recognize the different impacts of energy intake and energy expenditure on energy balance
Food intake elicits an increase in energy expenditure, known as the "thermic effect of food" (TEF). It is mainly due to the need to regenerate the ATP used for the absorption, transport and storage of the nutrients consumed (15). It is usually considered to amount to about 10% of the food energy consumed when living on a mixed diet. In addition, modest increases or declines in resting energy expenditure occur during periods of excessive or deficient energy intake, which are commonly referred to as adaptive thermogenesis (cf. #4). The sum of the latter plus TEF is often referred to as diet-induced thermogenesis. These changes can only slightly attenuate, but not reverse, the impact of changes in energy intake on the energy balance. Unfortunately, the energy balance equation suggests that energy intake and energy expenditure occupy equivalent roles in determining energy balance, when in fact the factors governing energy intakes influence the energy balance far more powerfully than the factors determining resting energy expenditure. This important fact does not become evident by a simplistic consideration of the energy balance equation.

8. Difficulties in understanding food intake regulation
In spite of the multitude of physiological phenomena known to contribute to the regulation of food consumption, variations in daily food intake are very large. The coefficients of variation for individual energy intake were found to average ±23% (16). Furthermore, changes in food intake are not closely synchronized with variations in energy expenditure, which can also be substantial (17). Evidently, metabolic functions can be readily sustained in spite of large daily deviations from energy balance. That is why evolution was not compelled to develop a precise control over daily food consumption. The physiological mechanisms involved in controlling food intake should therefore be expected to play only a minor part of the observed variability in daily food intake. This has made it difficult to elucidate the mechanisms involved. Furthermore, there appears to be considerable redundancy in this regulation. Thus, inactivation or stimulation at one control site may lead to temporary disruptions, but weight maintenance generally tends to become re-established subsequently, albeit possibly at a different level. Since most individuals maintain stable body weights during long periods of their lives (2), and since changes in resting energy expenditure cannot compensate for changes in intake (cf. #7), it can be inferred that food intake tends to adjust itself remarkably well to energy expenditure over the long term, even though large daily deviations from energy balance occur. Therefore, adjustment of intake to expenditure in humans must obviously be happening over periods of several days. This view is supported by the recent recognition of corrective responses occurring with 3–4-day delays (18).

Although less obvious than the fact that energy intake must be equal to energy expenditure, weight stability also requires that the substrate mixture
oxidized be equivalent, on average, to the composition of the nutrient mix consumed. When "substrate balance" is not achieved, changes in body composition occur, which in turn are bound to elicit adjustments in food intake (15,19).

The contributions made by carbohydrate and by fat to the fuel mix oxidized is reflected in the ratio of CO₂ produced to O₂ consumed. This ratio is known as the “respiratory quotient” or “RQ.” It varies between the values of 1.0, when CHO is the predominant fuel, and 0.7, when oxidation of fat provides most of the body’s energy. The ratio of CO₂ produced to O₂ consumed during the biological oxidation of a representative sample of the diet consumed is defined as the “food quotient” or “FQ” (15). Stable body compositions will only be sustained if the average RQ matches the average FQ of the diet.

The composition of the fuel mix oxidized and hence the average RQ are influenced by the size of the body’s substrate reserves. The steady state of weight maintenance thus tends to become established for a particular body composition in a given individual living under a particular set of circumstances. This corresponds to a "settling point" (20). Such a view accommodates the fact that circumstances cause weight stability to occur for various degrees of adiposity. Thus it seems to fit reality much better than the concept of a "set point" or "ponderostat" (21) often invoked to explain weight stability. In fact, such a concept would seem to be utterly inconsistent with the rise in the preponderance of obesity, since set-points would have to be seen as preventing the impact of changing circumstances. It has sometimes been considered that "set-points" are reset for different conditions, but in effect this argument reduces the set-point phenomenon to a settling point.

Rapid weight changes take place during growth, as well as sometimes in adults. Such changes reflect the fact that their body composition is still substantially different from that which corresponds to the steady state of weight maintenance.

10. Problems with the application of the RQ/FQ concept
An RQ greater than the FQ indicates that CHO makes a greater, and fat a smaller, contribution to the substrate mix oxidized than their relative proportions in the diet (3). On the other hand, a RQ/FQ ratio below 1.0 reflects the oxidation of a fuel mix containing a higher proportion of fat than that provided by the diet. While this insight is theoretically valid, the differences between RQ and FQ under conditions of variable nutrient intakes are small and greatly influenced by daily events. Except under tightly controlled conditions, the RQ/FQ ratio cannot be established with sufficient precision to predict whether weight gain or loss would take place. Reports finding no correlation between RQ/FQ data and body weight or body weight changes should therefore not be taken to challenge the validity of the RQ/FQ concept.

11. The "defense of body weight" concept
The common tendency of individual body weights to return to their original value after a weight-changing intervention is often explained as the manifestation of a mechanism tending to "defend" a particular body composition. The problem with this concept is that it appears to imply that mechanisms exist to actively drive the fat mass to a particular level, much as one would expect if a set-point mechanism existed (21). It fails to take into consideration that before the intervention, body composition for a given individual had already evolved until a steady state of weight maintenance had become established. The body composition that prevailed before such an intervention will naturally tend to re-establish itself when the disrupting intervention has ceased, not because a given adiposity is "defended" or "targeted," but because weight maintenance tends to become re-established at the settling point, i.e., at the particular body composition which that individual had previously reached under this set of circumstances (19).

Discussion of differing interpretation of such concepts as settling point, set point, ponderostat, and defense of body weight, which all appear to provide tenable explanations for common observations, may seem to be futile, until one tries to understand how environmental and dietary factors can influence adiposity and the preponderance of obesity.

12. The different roles played by carbohydrates and fat in energy metabolism
Dietary carbohydrates and fats both provide substrates for the regeneration of the ATP expended to sustain the body’s functions. Carbohydrates generally contribute 40–60% of dietary energy and daily CHO intakes in adults consuming mixed diets range from 200 g in relatively small and sedentary individuals to >500 g in physically active persons. The body’s glycogen reserves may be estimated to vary between 1.0 and 1.5 times the amount of carbohydrate consumed and oxidized during a typical day (22). The body’s fat
content commonly amounts to 10–15 kg, being much larger in obesity. The triglyceride reserve typically ranges from 100,000 to 200,000 kcal in adults and it is thus some 100 times greater than the CHO reserve of 1,000–2,000 kcal present in the form of glycogen.

Given its small size in relation to its turnover and the importance of maintaining adequate blood glucose levels, maintenance of appropriate glycogen stores present a considerable metabolic challenge. Evolution was therefore compelled to develop appropriate regulatory features to adjust glucose oxidation to carbohydrate availability, through adjustments of the activity of key enzymes and by hormonal signals, notably those conveyed by insulin and glucagon. Thanks to these, large variations in carbohydrate intake can be accommodated without noticeable stress. Other phenomena cause the oxidation of amino acids to adjust themselves to protein intake, as recognized long ago by monitoring nitrogen balances. On the other hand, the body’s large fat stores are hardly affected by daily gains or losses and adjustment of fat oxidation to fat intake has received much lower priority in metabolic regulation. Indeed, consumption of fat has little or no effect on fat oxidation, which declines even following fatty meals (23).

13. Food intake regulation and carbohydrate balance
Spontaneous food consumption is increased after periods of food deprivation, and inhibited after deliberate weight gain, but only until the status prevailing under the habitual ad libitum conditions is re-established. This makes it glaringly apparent that food intake regulation does not have maintenance of energy balance as its primary purpose. In addition, it becomes evident that body composition is an important parameter in the regulation of food intake (19).

Maintenance of appropriate glycogen levels under conditions of ad libitum food intake would be facilitated if, in addition to adjustment of glucose oxidation to carbohydrate intake, food intake were to be regulated in a manner helping to sustain the balance between the use of glucose and the influx of dietary carbohydrate. Making such considerations at a time when the existence of specific glucose receptors in the brain had just been revealed, Mayer (27) developed the concept of “glucostatic” regulation of food intake, in which it is presumed that monitoring of blood glucose levels by the brain generates signals for the regulation of food intake by the central nervous system. Indeed, it is now known that transient small declines in blood glucose levels tend to elicit feeding (28). However, blood glucose levels vary greatly during the day and there is much overlap between the values that prevail under different nutritional and metabolic conditions. Subsequently, it was therefore considered that changes in liver glycogen levels (29) or in liver substrate oxidation rates (30) would be more suitable or more likely to provide appropriate feedback signals to the brain, as such inputs can be based on some integrated parameter of substrate and carbohydrate utilization and availability. Little is known about the mechanisms and signals that may be involved, though there is a possibility that they could be transmitted to the central nervous system via the autonomous nervous system (31).

One could also entertain the notion that the rate of change instead of, or in addition to, the size of the body’s glycogen stores could provide signals affecting hunger. This would account for the fact that hunger is greatly attenuated after a few days of total starvation and relatively well tolerated on protein-sparing diets (32), once the organism has become adapted to low but stable glycogen and blood glucose levels.
14. The difficulty in obtaining experimental evidence about the role of carbohydrate balance in food intake regulation

In one of the few studies suitable to examine this issue, Stubbis et al. (33) used continuous indirect calorimetry in a respiratory chamber to established 24-h substrate balances in young men eating ad libitum over 7 consecutive days. They observed a negative correlation between 24-h carbohydrate imbalances and subsequent food intakes, which accounted for 5–10% of the variance in the next day's energy balances and hence energy intakes. Considering that most factors influencing food consumption and variations in the daily energy balance occur pretty much at random once a particular lifestyle has become established, even modest, but systematic, regulatory effects have the potential to exert significant long-term "steering effects." These may be difficult to establish with statistical certainty during the short experimental periods feasible in humans. The situation is similar to casino games, where the small percentage gains programmed for the house would be difficult to characterize in the short run, but lead in time to significant profits.

15. The need to distinguish between the role of carbohydrate balance in food intake regulation and the role of habitual glycogen levels in body weight regulation

Regulation of food intake in a manner helping to maintain carbohydrate balance provides means to achieve body weight stability, but only when the situation has been reached for which the composition of the fuel mix oxidized matches, on average, the nutrient distribution in the diet. However, in relation to body weights and health, the mechanisms involved in stabilizing body weights are less important than the factors determining the body fat content for which weight maintenance tends to occur.

Glycogen levels are spontaneously maintained at levels sufficient to prevent hypoglycemia and to carry out habitual physical tasks. They also spontaneously remain far below the level at which rapid conversion of carbohydrate into fat is induced in adults consuming mixed diets (12,13,34). Glycogen levels in adults can be estimated to vary between a lower limit of some 150–200 g and an upper limit of 500–600 g. Glycogen levels are known to be higher on high-carbohydrate than on low-carbohydrate diets (22). They are therefore not likely to vary over the entire range when conditions are stable, but to oscillate within a narrower range. Since neither the lower nor the upper limits are specifically determined, the range within which glycogen levels are habitually maintained can differ among individuals and be affected by circumstances as well.

Although actual measurements of glycogen levels in human populations are not yet available from which one could gauge the influence of glycogen levels in reducing fat oxidation, this effect can be recognized in experiments performed in respiratory chambers, where changes in glycogen content could be calculated (26,33). When the range within which glycogen levels are habitually maintained rises, daily fat oxidation can be expected to decrease, promoting fat accumulation. Thus, the role which increased habitual glycogen levels will play in promoting obesity in humans needs to be recognized! An attempt was made to assess the scope of this effect in a computer model of human metabolism that reproduces some of the behaviors known to regulate substrate utilization in humans (35). Minor upward shifts in habitual glycogen levels led to substantial body weight gains, whereas decline in glycogen levels entrained significant weight losses. The model's behavior thus supports the view that changes in glycogen levels too small to be documented by current means conceivably can explain recent gains in adiposity.

16. Understanding the recent increases in the preponderance of obesity

During the past few decades a continuing increase in the prevalence of obesity in the United States has occurred (36), even though neither the population gene pool nor the parameters considered to have caused the progressive increase in obesity in affluent societies, such as higher dietary fat content, greater buying power, and decreased physical activity, appear to have changed substantially during this period. However, food diversity and its appetizing qualities (37), changes in its energy density and increased portion size, wider choices, and advertising efforts have continued to increase. In various ways, these factors encourage food consumption so that higher glycogen levels are reached after meals. Furthermore, depletion of glycogen levels between meals is counteracted by the ubiquitous availability and promotion of appetizing snacks and caloric drinks. It will be readily appreciated that together these environmental changes are bound to raise the range within which glycogen levels are habitually maintained. By influencing the size of the fat mass necessary to cause fat oxidation to be commensurate with fat intake, shifts in "habitual glycogen" levels modify the steady-state conditions, although the
mechanisms regulating food intake remain the same. The quantitative impact of raised habitual glycogen levels has been examined in a computer model built to reflect the overall interactions between glycogen levels and fat stores in humans. It indicates that an increase by 25g in the range within which glycogen levels are habitually maintained would require an increase in body fat content of 5% to restore fat oxidation to the previous level, which would correspond to a weight gain of some 7 kg and an increase of about 4 in the BMI (BMI = Weight (kg)/(Height (m))^2 (ref. 35).

17. Why don’t people eat even more?
In humans, restraint on food intake can be due to conscious efforts, to a degree susceptible to cultural influences and to the prevailing level of adiposity in the public. Unfortunately all such efforts fail too frequently to prevent excess weight gain. It would appear that in a large segment of the population, control over food intake is largely dependent on physiological mechanisms. These don’t appear to have been shaped by evolution to prevent excessive weight gain in conditions of an overabundant food supply, but can become effective once the fat mass has enlarged. A number of signals influencing food intake originate in the gastrointestinal tract and others are elicited by circulating substrate and hormone levels. For the most part, however, these decay overnight and do not carry over much information from one day to the next (38,39). Furthermore, these signals are commonly thought to be more powerful in preventing energy deficits than weight gain (40). Other mechanisms must therefore be at work in modulating food intake from one day to the next. In particular, it is evident that even when highly desirable foods are readily available, people eat substantially less on most days than the amounts that they readily consume on high-intake days (41). Even among individuals who appear to combine dietary and lifestyle habits believed to promote the development of obesity, weight gain over the years is much slower than one would expect considering the pleasure associated with eating, the loose regulation of daily food intake, and the great tolerance for excessive intakes. We know little about the phenomena limiting food intake, but their power is made evident by the weight loss that spontaneously takes place after periods of deliberate overfeeding (42–44). Further evidence can be seen in the fact that there is no correlation between adiposity and stature, even though resting and total energy expenditure are positively correlated with stature (45) and many meals of standard size are served to short and tall people (5).

Adjustments of food intake related to gains or losses of glycogen can be expected to result in a "modulation" of intake, effectively serving to maintain glycogen levels sufficient to prevent hypoglycemic events, while remaining far below the levels at which appreciable de novo lipogenesis would be induced. Thus, the regulatory effects serving to limit glycogen accumulation offer a potential and plausible mechanism for restraining food intake when faced with an unlimited supply of appetizing foods, but only once the average rate of fat oxidation matches the average fat intake.

18. Confusion about the effect of exercise on the energy balance
Regular physical activity effectively reduces the likelihood of developing obesity (46), and the recommendation to increase exercise as a means of controlling body weight is constantly emphasized to sedentary individuals (47). However, it has been difficult to find a consistent explanation to account for the fact that exercise causes a negative energy balance in some situations but not in others. The issue is complicated by the fact that physical exertion causes major perturbations in metabolism, as it demands rapid and intensive fuel mobilization to provide the substrates needed to sustain ATP regeneration. Furthermore, exercise affects metabolism beyond the period of physical activity itself. It causes the so-called "excess postexercise oxygen consumption" (48), as well as changes in substrate utilization.

What can be said is that in the absence of exercise, increases in the adipose tissue mass are often required to raise fat oxidation to a rate commensurate with the diet's fat content. The synergistic effect of high dietary fat and lack of exercise in promoting obesity is well illustrated in children. Their spontaneously high physical activities used to limit childhood obesity, until increasing inactivity caused a rise in its prevalence (49).

Since exercise leads to a steady state of weight maintenance at lower levels of adiposity, it can be inferred that exercise enhances fat oxidation more than CHO oxidation (50). This is the case even though glucose often makes a major contribution to the fuel mix oxidized at the onset of exercise, as this is evidently compensated later by an increase in fat oxidation (51). Thus, introducing physical activities into the daily routine enhances fat oxidation relative to CHO oxidation. Furthermore, physical training increases the body's ability to use more fatty acids and less glucose (52).

Thus, the additional amount of food needed to maintain CHO balance is then less than the...
exercise-induced increase in energy expenditure, resulting in weight loss. In individuals who have reached a steady state accommodating the impact of habitual physical activity on fuel metabolism, eating to maintain glycerene levels then again provides fat calories in amounts appropriate to maintain energy balance. With these considerations in mind, one can readily understand why exercise sometimes induces negative energy balance and sometimes does not (50).

In the computer model cited above (35) the impact of exercise is brought about by the greater glycerene depletion induced by exercise between meals. The relevance of this explanation can be appreciated simply by considering meal-to-meal intervals in terms of calories burned, rather than in terms of time elapsed. In a corollary manner, the model shows that consumption of snacks between meals, by sustaining higher glycerene levels between meals, leads to increased fat accumulation (35).

19. Is dietary fat or is dietary CHO the major culprit in causing weight gain?
In view of the considerations made above, it is not surprising that a high incidence of obesity is typically encountered in sedentary populations consuming diets providing substantial amounts of fat. As shown recently for free-living and unrestricted eating conditions, energy intakes are positively correlated with the fat content of the foods consumed on a particular day (18). In most animal models high-fat diets similarly promote fat accumulation.

This underlying epidemiological evidence appears to be contradicted by the often remarkably good weight-losing results achieved on regimens severely restricting CHO but not fat intake, such as the Atkins-type diets. It is important here to distinguish between situations of acute weight reduction, where intake is controlled by a specific diet plan, and long-term efforts to control or reduce body weights. In regard to the latter, numerous testimonials report that reducing dietary CHO leads to weight loss, while other individuals experienced weight loss by limiting fat intake. This leads to the conclusion in the first case that CHO, and in the second case that fat, is the dietary component most responsible for excess fat accumulation. Such conflicting impressions, often promoted with much publicity, have caused great confusion in the public. However, these seemingly contradictory conclusions can be accommodated simply by realizing that severe restriction on the consumption of any major macronutrient has the effect of substantially reducing the selection of desirable foods from which to partake. This will reduce the incentives to overeat (37), even without having to engage in formal "calorie-counting!"

Thus the answer to the question asked above is that the major culprit is the unrestricted and ubiquitous availability of a mixed diet, offering numerous appetizing foods, often in large portions, in which sugar, and to an even greater extent fat, contribute to raise the energy density.

20. How can inherited traits influence body weight regulation?
One can readily appreciate that inherited personality traits, as well as learned and cultural behavioral traits, will influence food selection, one's ability to control eating behaviors, the tendency to engage in physical activities, and thereby steady-state adiposity. There is no reason to think that the way in which the organism is poised in regulating the relative use of CHO and fat should not be affected by inherited metabolic and hormonal differences (53). Indeed, in "high CHO-burners" a greater expansion of the fat mass is needed to achieve a given proportion of fat-to-CHO oxidation. It has indeed been observed that persons maintaining relatively high ROs under standardized conditions are likely to be affected by greater subsequent weight gain (54,55). This effect is likely to be magnified when dietary CHO is accompanied by substantial amounts of fat. An inherited or permanently acquired effect affecting the mechanisms regulating the sparing effect of glucose on fat oxidation, and vice versa, should be expected to exert a potentially powerful leverage on body weight regulation. Indeed, this is clearly demonstrated in the two-compartment computer model (35). On the other hand, one should not expect adiposity to be much influenced by genetic effects causing resting metabolic rates to be higher or lower than the average (6).

21. The leverage of inherited vs. noninherited factors
The relative impacts of inherited and noninherited factors on body composition are commonly judged by the contribution that they make to the variance around the mean of BMI data. However, this does not appropriately recognize the impact of factors causing shifts in the means. To take such shifts into account, it is useful to subdivide the noninherited factors into those determining the general environment in which a population lives, i.e., the "environmental factors," and those affecting an individual's condition within this population, which may be described as the "circumstantial factors."
The importance of this distinction is that environmental factors can shift the means. For example, the mean BMI (±s.d.) of Nigerian men living in Nigeria was reported to be 21.0 ± 4.2 when living in Nigeria, whereas it was 27.0 ± 5.4 when living in Chicago (56). The data summarized by Costa and Steckel (57) show the average BMI of adult men in the United States as rising from 22.5 in 1894 to 23.6 in 1944, and to 25.7 in 1991. While variability about the means reflects equal proportions of values higher and lower than average, environmental forces capable of changing the mean have a unidirectional impact. The latter is bound to have a more powerful influence on the proportion of individuals whose BMI will exceed certain limits than the variations about the mean attributable to circumporal factors, such as socioeconomic and lifestyle variables. Thus, environmental, circumstantial, and genetic factors contribute in different ways to adiposity and to the obesity epidemic. In most situations, only the circumstantial factors should be thought to be controllable by individuals. Strategies for weight control should take this into account by offering opportunities to strive for weight control within families or in group settings. This could provide a helpful measure of change in an individual's environment. Encouraging the development of physical activity habits, notably in children and adolescents, also offers the potential for "improving" the environment, if they could become a routine in a population.

22. BMI vs. % ideal body weight

For many decades, body weights were assessed relative to "ideal body weights" (IBW), i.e., the weight associated with the longest life expectancy, as judged from life insurance data. It requires the use of tables giving IBW as a function of height. This has now been supplanted by the use of the BMI, which does not require such tables. In its simplicity, BMI is well suited to establish epidemiological data. A BMI between 25 and 30 indicates overweight, and BMI >30 obesity. However, the BMI is a highly abstract notion and information in terms of the BMI does not convey nearly as much information to individuals and patients as learning how their weight relates to IBW. Does their weight fall into the 20-40% above IBW range indicative of overweight, or by how much does it exceed the 140% of IBW value corresponding to obesity? Now that hand-held computers can be easily programmed to generate % IBW data (which could be upgraded to take age into account), one could again consider informing patients about their weight status according to the more understandable, and potentially alarming, % IBW criterion.

Conclusions

The problem of body weight regulation and obesity ultimately boils down to two questions: (i) what are the mechanisms which operate to correct the imbalances created by the large short-term variations in energy intake (cf. #8, 13-15,17), whether they result in exact energy balances or in slow rates of gain or loss of fat over time, and (ii) why is the state of approximate weight maintenance reached for such widely differing levels of adiposity (cf. #2-7, 9-12, 15-16,18-21)? This second issue is one of practical significance, but it must be addressed in a manner consistent with the mechanisms that bring about weight stability. A plausible explanation, compatible with this condition, can be proposed to account for the recent increase in the preponderance of obesity. It attributes the influence of the food supply to its effect in raising the range within which glycogen levels are habitually maintained. Furthermore, it seems important to overcome several misconceptions that appear to stand in the way of a better understanding of weight maintenance. This may ultimately help in learning how to enhance the effectiveness with which the physiological regulation of food intake and conscious efforts are capable of attenuating environmental pressures to overeat.

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