

1990

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Recommended Citation

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Obesity

A Biobehavioral Point of View^a

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If you ask an overweight person, "Why are you fat?", you will, almost invariably, get the answer, "Because I eat too much." You will get this answer in spite of the fact that of thirteen studies, six find no significant differences in the caloric intake of obese versus nonobese subjects, five report that the obese eat significantly less than the nonobese, and only two report that they eat significantly more.

It is hard to overcome this possibly incorrect belief about the cause of obesity when most practicing professionals and certainly every diet book is based on the assumption that excessive caloric intake is at fault. In spite of a failure rate approaching 90 to 95%, we still cling to dietary exhortations in our treatments, and suspect that lack of adherence to our recommendations is responsible for failure.

Recent research in the field of biochemistry suggests that several newly discovered factors, as well as others that have been known for years but generally overlooked, may contribute to obesity in a way that is not easily remedied by dieting. Caloric restriction may lead to an adaptive metabolic response that reduces a person's daily energy needs, and to hormone and enzyme changes that lead to an enhanced rate of fat storage following caloric restriction. Adaptive responses may be associated with initial dispositional tendencies for some individuals to be heavier than others, and, together, these adaptive and dispositional tendencies may provide a basis for the continual frustration experienced by millions of persons who repeatedly diet to lose weight.

We will review evidence for these adaptive and dispositional tendencies that resist weight loss efforts and then suggest an alternative approach to severe caloric restriction based on data from the Vanderbilt University Weight Management Program.

^a The authors are supported by Grants #MH14757 and #MH08709 administered by the National Institutes of Mental Health.

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DISPOSITIONAL AND ADAPTIVE TENDENCIES TOWARD OBESITY

Although it is hard to disentangle the effects of learning and the environment from the influence of heredity, the role of genetic influences can be clearly demonstrated in both single- and multiple-gene obesities in animals.² The most convincing evidence for a strong genetic component in human obesity is presented by Brook³ and Brook, Huntley, and Slack,⁴ who determined that the correlation between tricep and subscapular skinfolds for monozygotic twins was 0.72 and 0.83, respectively, compared with 0.49 and 0.34 for dizygotic twins. Borjeson⁵ compared skinfolds at three sites and found that the average intra-pair differences were three times greater in dizygotic twins than in monozygotic twins. He concluded that the coefficient of heritability was somewhere between 0.50 and 0.88.

A multitude of other studies could be cited to illustrate that there is no longer any argument about the existence of a genetic component that influences the relative ease with which the human body stores fat—the question now becomes, Through what diverse physiological and biochemical mechanisms can it be manifest, and how may these mechanisms be modified, or how can we compensate for them, by changes in our diet and activity habits when it seems desirable to do so for physical or psychological reasons?

Biochemical Mechanisms

Several biochemical mechanisms have been identified that might lead to a between-persons dispositional basis toward obesity. Each of these mechanisms may also respond differentially to overfeeding or underfeeding with respect to an established weight in any given person. Although the boundaries limiting the operation of these biochemical mechanisms are set genetically, there is little doubt that lifestyle differences also affect their operation just as the expression of many genetic potentials depends upon an interaction between an organism and its environment. Thyroid deficiency, operative supposedly in but 5% of the population, is only one of many factors. Variability in other hormones and nerve transmitters that can affect appetite, fat storage, and fat utilization include insulin, the catecholamines, endorphins, serotonin, and dopamine. Enzymatic differences, most strongly verified in animal research, include $\text{Na}^+, \text{K}^+ \text{--ATPase}$, lipoprotein lipase, and various others involved in brown fat thermogenesis, the glycerol phosphate shuttle, and substrate cycling. Central nervous system differences, located especially in the hypothalamus, have been noted in association with these hormonal and enzymatic differences.

All of the biochemical factors are associated with energy utilization. In performing their functions, they can either conserve or waste energy. They provide the biochemical foundation underlying statements such as “all I have to do is look at food and I gain weight” to “he eats everything in sight

and never gains an ounce.” The first person has a very efficient body—it wastes very little energy performing the work it has to do to stay alive and should that person overeat in the presence of an abundance of food, it will put a large percentage of the overage into its fat banks. The first person is well equipped to withstand the famines that still frequently plague a large percentage of the human race. The second person has an energy-inefficient body. If he overeats, the body simply turns on one of the possible mechanisms to waste the overabundant energy. He is not well equipped to withstand a famine, but he is protected against obesity in times of plenty.

Brown Fat

In an extensive series of studies with rodents, Rothwell and Stock^{6,7} and a number of other investigators have established brown fat as a key factor in metabolic functions related to obesity (see McMinn⁸ and Morgan & Goldberg⁹ for reviews). Brown fat, in contrast with ordinary, “white” fat, is highly vascularized and does not function as a storage depot for excess energy. Instead, brown fat plays a central role in diet-induced thermogenesis and cold adaptation. When normal lean rats and mice are overfed, brown fat can increase in mass and in heat production such that a major portion of excess calories is wasted in heat. The genetically obese varieties lack this adaptive mechanism.¹⁰⁻¹² The fat prone animals gain considerable weight—they can double in fat content, while the lean may gain about one-third the fat that might be expected from the amount of food ingested above energy needs.¹³ In addition, in the normal rat, the brown fat remains active when regular feeding is resumed until the extra store of ordinary fat is burned off and normal weight is re-established.

Although the major research has been done with animals, the presence of brown fat in humans has been verified. Of course one cannot assume that it plays an identical role in human predispositions to obesity, but if brown fat is distributed in mass and in function with the great variability that we see in other human attributes, and suitable investigatory techniques can be devised, future studies may reveal at least some role for this tissue in human obesity.

Adipose Tissue Lipoprotein Lipase

Adipose tissue lipoprotein lipase (AT-LPL) has already been implicated in both animal and human dispositions to obesity. AT-LPL resides on the membranes of fat cells and breaks down triglycerides for storage. Elevated levels of lipoprotein lipase activity have been reported in the fatty strains of both rats¹⁴⁻¹⁶ and mice.¹⁷ Cleary, Vasselli and Greenwood¹⁸ have shown that AT-LPL is active without hyperphasia, that is, elevation of AT-LPL activity occurs when genetically obese animals are prevented from overeating. Under these conditions, lean tissue is robbed of nutrients in order to accumulate excess adipose tissue. Schwartz and Brunzell¹⁹ found a correla-

tion of 0.91 between AT-LPL activity and body weight and 0.71 between AT-LPL activity and fat cell size in humans. At least in part, AT-LPL activity is stimulated by insulin, but it can apparently be active independently of that hormone, at least in rodents.

When a person goes on a diet, AT-LPL activity is reduced; the amount of reduction appears to increase over time in all subjects. However, research with humans, notably that of Schwartz and Brunzell^{19,20} and Taskinen and Nikkila,^{21,22} has demonstrated that AT-LPL activity is less reduced during a period of caloric restriction in obese subjects than in nonobese subjects. Thus, as time goes on, it may become increasingly harder for obese subjects to lose weight. Then, after the termination of a low-calorie diet (e.g., 600 calories in Schwartz & Brunzell¹⁹), AT-LPL activity will increase many-fold over baseline, three times on the average but as much as six to eight times in some cases. These biochemists use the word "pull"—it is as though the fat cells were pulling the substrate right out of the blood stream. When subjects regain all of their weight (usually even a bit more than they lost to begin with) AT-LPL activity returns to normal or near normal. However, at least for 8 to 14 months after weight loss, it can remain elevated in activity as long as the subject struggles to maintain a lower weight.^{19,23}

Na⁺,K⁺—ATPase

Differences between lean and adipose rodents in the activity of the enzyme responsible for the sodium pump, Na⁺,K⁺—ATPase, have been reported in a series of studies by Lin *et al.*^{24–26} The amount of thermogenesis dependent upon the activity of the sodium pump has been estimated repeatedly, with results ranging up to 40% of the total energy required for basal metabolism. So, if obese mice have less Na⁺,K⁺—ATPase activity, a thermic mechanism involving sodium pump activity must be considered in understanding the etiology of obesity.

Studies with humans have been less definite than animal studies, however. Consistent with the results of animal studies, DeLuise, Blackburn, and Flier²⁷ reported less Na⁺,K⁺—ATPase in the red blood cells of obese humans compared with persons of normal weight. This finding was countered by a later report showing greater enzyme activity in the liver of obese humans than in the nonobese.²⁸

Future investigations with human subjects are needed to determine which tissue is most appropriate for measuring Na⁺,K⁺—ATPase activity. It is of great potential importance in both adaptive and dispositional differences in metabolic activity. It is intriguing to note that Rothwell, Stock, and Wyllie²⁹ found a remarkably high correlation (0.91) between brown fat activity and Na⁺,K⁺—ATPase activity within brown fat. However, much more research is needed to determine in what species and within what tissues Na⁺,K⁺—ATPase activity varies, since the liver tissue of fatty rats does not appear to differ from normal.³⁰

Other Enzymes

Other mechanisms that contribute to either adaptive or dispositional weight gain have been suggested but have not been followed up because of various difficulties in pursuing such research. Galton and Bray³¹ and Bray³² reported evidence for the possible role of the glycerol phosphate shuttle in human obesity. One enzyme in the shuttle may be less active in persons with a genetic tendency toward obesity and in persons who have adapted to a diet. The inactivity of this enzyme may lead to greater energy efficiency in the oxidation of NADH and may also lead to greater fat formation since glycerol phosphate is more readily available.

The role of substrate cycling has been implicated, in theory, as a potential contributor to metabolic variation.^{33,34} Specifically, an intermediate step in both glycolysis (glucose breakdown) and gluconeogenesis (glucose production) may cycle in a futile manner and thereby waste energy. After dieting (or in persons with a tendency toward obesity) the activity of the substrate cycling may be reduced. The empirical evidence for the role of substrate cycling in obesity is very limited.

ADAPTIVE METABOLIC RESPONSE TO DIET

The exact relationship of changes in metabolic rate to changes in caloric intake is not known with any degree of precision. That is, we cannot predict to what extent metabolism may slow in relationship to increasing amounts of caloric restriction in any individual case. Bray³⁵ states that adaptation will occur almost invariably when intake is reduced to 800 calories per day, but it is likely that in some persons metabolic changes follow energy intake variations quite closely.

A study by Benedict, Miles, Roth, and Smith³⁶ revealed a fall in BMR, resting pulse rate, and body weight for a group of healthy, normal weight volunteers placed on a calorie-restricted diet approximately eight weeks before Thanksgiving. The fall partially recovered in two holiday "times out" during Thanksgiving and Christmas. Then, with increasing rapidity, it returned to a lower level when the low-calorie diet was resumed. After losing an average of approximately 7 kg, weight appeared to stabilize at an intake roughly two-thirds of baseline levels, with about a 20% average reduction in BMR.

When the subjects returned to *ad libitum* eating, weight was regained between two and three times faster than the speed with which it was lost.

In a more recent study, DiGirolamo, Smith, and Bjorntorp³⁷ found that rats fasted for a three-day period in which 10% of body weight was lost required only 60% of their former energy intake to maintain their lowered weight for at least a 13-day period.

Summarizing from the many investigations reported in Bjorntorp, Cairella, and Howard,³⁸ it appears that the CNS command headquarters in charge of metabolic adaptation lies in the hypothalamus, which organizes

CNS activity to regulate thermogenesis. Upon caloric restriction, CNS activity at various sites, probably including skeletal and heart muscle and brown fat depots, is reduced. For example, CNS activity and norepinephrine turnover is reduced in the heart muscle of rats during caloric restriction.³⁹ Other signals, relayed through some complex network not as yet entirely understood, result in less fat being incorporated into adipose tissue while following a low-calorie diet.

Metabolic adaptation to a low-calorie diet begins within 72 hours, and proceeds to reach maximum within three to seven weeks. Speed of weight loss slows, both as initial glycogen stores are depleted (along with the large amount of water with which the body's glycogen is stored) and as metabolic adaptation sets in.

When *ad libitum* feeding is resumed, there is a rapid rebound effect, owing in part to the reduced caloric needs relative to intake, the rapid refilling of depleted glycogen storage sites, and the rebuilding of any wasted muscle mass that may have occurred as the body burned some of its own protein stores in order to create needed glucose for energy. For every gram of glycogen restored to the liver and muscles, and for every gram of protein incorporated into muscle tissue, approximately 3 to 4 grams of water are also integrated into the system.

In addition, restoration of additional calories in carbohydrate to the diet appears to turn on a mechanism, apparently related to an increased secretion of insulin necessary to handle the incorporation of increased energy into body cells, that causes sodium retention, and therefore water retention, which for a period of time may actually overcompensate for the previous dehydration and lead to edema.

It is evidence like this, together with the easily observable fact that most people who lose weight by dieting do indeed put it all back in spades within two to five years, that has rekindled interest in what has been called "set-point" theory. As Bennett and Gurin⁴⁰ put it, set-point theory claims that physiological/biochemical mechanisms, set by your genes, act to determine what you will weigh "when you are not thinking about it." If you try to change, certainly if by dieting alone, forces are set into motion to counteract your efforts. We have presented only a small fraction of the evidence that has been marshalled to support the set-point notion. However, as will be discussed shortly, set-point theory is best interpreted as a range within which lifestyle factors, such as exercise and diet, work to adjust body weight.

WHAT DOES IT TAKE TO BE A SUCCESSFUL LOSER?

We will focus here on the issue of greatest importance, and that is, not what it takes to lose weight in the first place, but what it takes to keep it off once a person has lost it.

Follow-up research with successful losers—persons who are keeping their weight off after using low-calorie commercial weight loss plans that do not emphasize increasing physical activity—suggests that caloric require-

ments are reduced as a consequence of such diets. After losing weight on diets of from 330 calories to 800 calories per day, women's caloric needs, given a sedentary lifestyle, appear to stabilize during the first year of follow-up within the area of 1200 to 1300 calories per day, while men's stabilize between 1600 and 1800.⁴¹ These caloric intakes, taken from weekly eating diaries of persons who are maintaining their losses and from the maintenance programs prescribed by various diet centers, are between 30 and 40% below the average daily requirements, for persons of average weight, estimated by the Food and Nutrition Board of the National Research Council.

The Vanderbilt Weight Management Program, in contrast with most commercial programs, emphasizes physical activity at least equally with sound nutrition. We have customarily recommended a balanced 1200-calorie reducing diet for women and 1800 for men, together with building up to an average of approximately 45 minutes of extra physical activity per day equivalent to brisk walking. Our emphasis on physical activity as the key ingredient necessary for permanent weight management has, until recently (e.g., Bennett and Gurin⁴⁰) been unique in the field. In fact, from a theoretical standpoint, some noted investigators have concluded that exercise is an impractical component to treat.⁴²⁻⁴⁵ They point out that physical activity comprises a very small part of the daily energy expenditure in the Western World—that is, in relation to our basal metabolic energy needs and the energy used during our hours of work, other physical activity plays a minor role. They go on to say that it seems more reasonable to make dietary adjustments than activity adjustments to return to, and to preserve, desirable weight.

We believe this view completely misses the critical role that physical activity plays in weight management. To begin with, health professionals, along with the overweight persons they treat, think first about weight loss because it has to occur first in time and is uppermost in everyone's minds. An increase in activity seems to be a poor way to get that satisfying quick weight loss most overweight persons desire. And health professionals are often just as impatient as the persons they seek to help. They fear that they will lose their clients if weight loss does not proceed rapidly, and sometimes they feel pressure from professional colleagues who review papers submitted for publication to demonstrate large losses in a short period of time.

Because it takes about 35 miles of walking or running to burn enough calories to *lose* a pound of fat, it seems much easier to go on a low-calorie diet and lose that pound overnight (and maybe even two or three) without the need for uncomfortable vigorous exercise. Assuming no change in caloric intake, it would take at least 1750 miles of extra walking, and perhaps more as caloric needs drop with weight reduction, to lose 50 pounds of fat. How many overweight people are ready to start a walking program with that ultimate distance in mind?

This view of exercise in weight control completely misses its singularly important role. Let us examine the apportionment of energy expenditure in a woman about 50 pounds overweight, weighing perhaps 175 pounds,

needing approximately 1800 to 2000 calories per day to maintain her weight. Of her basal metabolic needs, perhaps 200 is going toward the maintenance of her excess adipose tissue. Compared with the organs that use the majority of our calories in the resting state—the heart, central nervous system, lungs, liver, kidneys, and skeletal muscle system—fat is relatively inactive tissue, and it may take as little as 200 calories a day to support as much as 50 pounds of fat. During the process of weight loss, this woman can solve the problem of *weight maintenance* if she will learn to expend 200 additional calories a day in her skeletal muscle system. Then, when she reaches desirable weight, if she can continue to burn up 200 additional calories each day, she will be able to return to some approximation of her earlier level of caloric intake, and not put any of her weight back on again. She is now burning the number of calories that previously went to the support of excess fat tissue to the tune of 50 pounds. Just three miles per day of extra walking, or its energy equivalent, can keep her from slowly regaining the weight she has lost. Thinking in terms of just three miles per day for *weight maintenance* is a much different proposition from thinking in terms of 1750 miles of walking to *lose* 50 pounds.

That is the singularly important role of physical activity in weight control.

Of course, metabolic needs and other dispositional factors toward a heavier than average weight, discussed previously in this paper, may require considerable differences in extra energy expenditure on the part of some persons if exercise is to play a major role in permitting food intake to approach the average of persons not predisposed to obesity. The data presented in FIGURE 1 illustrate this variability in persons who have lost significant amounts of weight and maintained their losses for at least five years using physical activity as their key maintenance behavior rather than dietary restriction.

FIGURE 1 presents the complete range of variation in the adult lives of five persons whose biological predispositions, given their previously sedentary lives, established what Bennet and Gurin⁴⁰ refer to as a “set-point” at the top of the depicted range when eating without restraint. Present weight is indicated by the cross bars at the lower end of the ranges.

The first woman (over 40 pounds lighter than her highest weight six years ago) averages approximately 1860 calories per day, adding about four miles of either walking or jogging to the baseline requirements of about two miles of movement in her work and other responsibilities.

The second woman (over 50 pounds lighter) maintains her weight at about 1915 calories, provided she adds 20 minutes every day of continuous free-style swimming to an otherwise sedentary existence.

The third woman maintains herself at about 1905 calories averaging about seven miles of walking every day.

These data are obtained from eating and activity diaries kept as part of our follow-up research from a select cadre of former participants each year.

Today, these three women all fall within normal limits of energy needs, *provided* they add the amount of activity that might have been required of

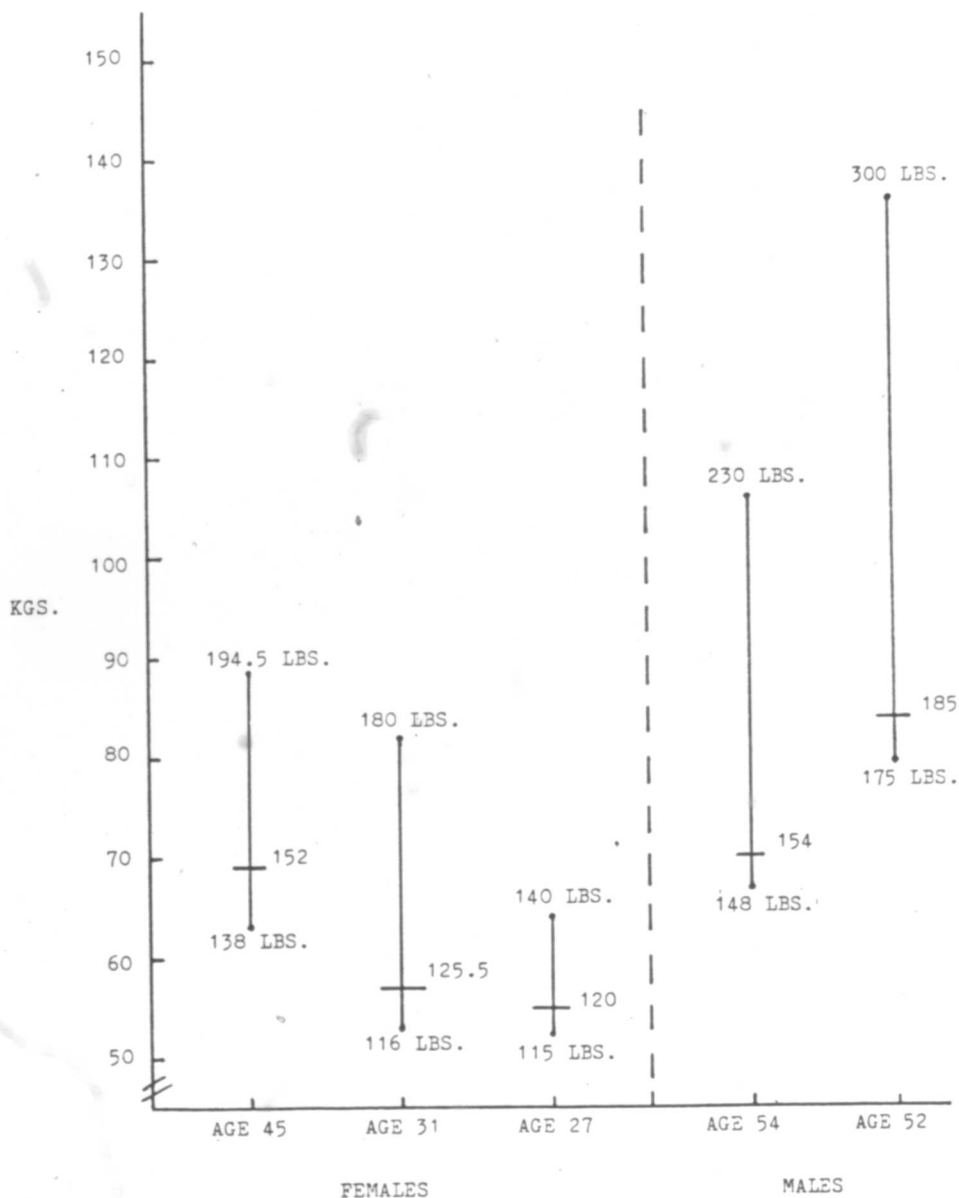


FIGURE 1. Weight ranges in their adult years of five formerly obese persons who have maintained significant weight losses for at least five years (present weight indicated by cross-bars).

them in their daily lives a few generations ago. Without that level of activity there is no doubt that their caloric needs at desirable weight would be reduced to the levels (1200 to 1300) reported earlier in this paper for persons who have used low-calorie diets and who are presently relying on dietary restriction for weight control.

The first man illustrated in the figure once weighed 230 pounds. He now maintains himself at 2960 calories per day with 35 to 40 miles of jogging, and tennis once or twice a week. He has a sedentary job, and without extra

physical activity his total amount of walking would rarely exceed two miles per day. However, his physical activity level puts his daily caloric requirements several hundred calories higher than the average inactive male of his age.

The second man provides an example of what it might take in the way of physical activity for a person with extreme tendencies toward obesity. His is a "high set-point" range. He lost 125 pounds on an 1800-calorie diet combined with what most overweight persons would consider an unbelievable increase in physical activity. He maintains his present weight on approximately 2600 calories per day and a weekly average of 35 miles of jogging, four hours of racquet ball, five hours on an exercise bicycle, and one and one-half hours of weight training. He no longer drives to work or to appointments near his office and averages about five miles per day of additional walking. His is the sort of genetic predisposition toward obesity that normal amounts of food would return to a grossly overweight condition; without his present amount of activity, the maintenance of desirable weight might require a daily intake of perhaps 1600 calories, just as we have observed in men who are relying on caloric restriction to maintain their weights after low-calorie diets. In such "high set-point" cases, we should not deceive ourselves—it will take a heroic effort in the way of physical activity to compensate and permit such persons to approach the food intake characteristic of the average.

Our files contain follow-up data on weight changes and level of physical activity for two years on 330 persons (87% women) who have participated in the Vanderbilt Program. Groups have been led by various persons, including professional staff, graduate students, and weight management specialists (paraprofessionals, all formerly overweight, who have been trained in sound nutrition, physical fitness, and group leadership skills). Among all groups, the correlation between weight loss from the date of entry in the program to follow-up ranges from 0.15 to 0.40 with amount of increase in physical activity, as determined from ratings obtained from interviews and follow-up questionnaires. Leaders who emphasized physical activity to a greater degree in treatment seem to have the groups in which the correlation between long-term weight loss with physical activity is highest.

However, in spite of what we feel is the proven value of physical activity in weight control, we are still failures when it comes to getting morbidly overweight persons permanently committed to the level of activity that is required. For example, in one group of severely obese participants (mean = 108 pounds above desirable weight, $n = 44$) that was led by one of the authors (MK) together with Dr. John Please, codirector of the program, only 39% were active at the recommended extra 200 calories a day at a 15-month follow-up, and only 15% had stayed consistently active at that level throughout 27 months of follow-up. Indeed, weight loss was highly related to activity level, with those persons equalling or exceeding 200 calories a day of extra activity (usually 45 minutes of walking) maintaining a mean loss of 46.7 pounds, compared with only 18.5 pounds for the less active

persons (see Katahn, Please, Thackrey, and Wallston⁴⁶ for a more complete description of this research).

In the larger sample of 330 persons who averaged in the vicinity of 50 pounds overweight on entry to the program, we find 20% consistently active over two years of follow-up. They are maintaining over twice the mean weight loss (13.37 pounds vs. 6.05 pounds) compared with those persons who do not meet the 45 minutes per day of movement that we so strongly encourage.

Because of the adherence problem, we now (since fall, 1982) approach weight management from a maintenance perspective, rather than a weight loss perspective. At the onset of the program, participants are helped to set up a program of physical activity that they feel they can stick with for life before we encourage any caloric restriction to speed weight loss itself. While we are working on the activity component, we also present sound nutritional information and use eating diaries to illustrate what it will take to lose weight and then to maintain desirable weight once it is reached. A large percentage of persons begin to lose weight "without dieting" at a satisfactory rate. Those who do not are helped to design a balanced, calorie-restricted diet that will achieve a loss of at least one pound per week. While a full year follow-up on our 1982-1983 participants is not yet available, a check on eating and activity records from our groups indicates that at least half are sustaining the recommended energy expenditure of 200 calories a day, or more, of physical activity after seven months.

In summary, we have reviewed a number of the biochemical mechanisms that help explain why obesity cannot be easily remedied by dieting. Short of surgical intervention, and possible discoveries in the way of acceptable long-term pharmacological interventions, an increase in physical activity seems to be the only way to maintain desirable weight after weight loss has been achieved through a combination of a temporary, sound calorie-restricted diet and exercise. Adherence remains a major problem, as well as designing schemes to help more people remain motivated to reach desirable weight, after which extra physical activity can play its key role in maintenance.

Furthermore, at the present time it is not known to what extent physical activity can alter the action of the predisposing biochemical factors that we have discussed. Past research indicates that certain changes do occur with activity that may reduce fat storage potential. For example, insulin levels are lowered, oxidative capacity of muscle tissue and myoglobin content increase, muscle cell mitochondria increase in number and larger amounts of glycogen are stored in active muscles, serum lipids and cholesterol levels may be reduced, and sensitivity to fat-mobilizing hormones increases.^{47,48}

But optimism over the ultimate potential of increased physical activity must be tempered with caution, especially and unfortunately in the case of obese women who seem to be under the greatest social pressure of all to lose weight. As Després *et al.*⁴⁸ report in their study of body composition and lipolysis, exercise may not achieve similar fat loss, and fat-mobilizing hormone changes in women as it does in men. The male body appears

genetically programmed to respond with adaptive fat-burning and fat loss changes to physical activity, while the female body may resist changes in its fat storage capacity in the face of exercise just as it resists changes to diet more "successfully" than the male.

The overall paradigm for future research in the area should include investigations of various levels of caloric restriction and physical activity on the rate of loss, future weight maintenance, and the biochemical reactions to such combinations. We are making a start in this direction in our own laboratory, using animal analogues of human methods of weight control, that is, varying the nature of the diet and amount of exercise, and then examining the activity of AT-LPL, the enzyme that may be responsible for the accelerated storage of fat after a low-calorie diet.

We look forward to making a report on this research in the near future.

ADDENDUM

In the time intervening between the presentation on which this article is based and its final preparation for publication, the authors have become aware of additional research that sheds further light on dietary and biochemical factors that may help us in our understanding and treatment of obesity.

One series of studies⁴⁹⁻⁵³ suggests that (1) under normal conditions very little dietary carbohydrate is converted to body fat, (2) short bouts of carbohydrate overfeeding lead to increased glycogen (not fat) storage and an increase in metabolic rate, (3) one must remain in positive energy balance for a considerable period of time before significant amounts of carbohydrate are converted to fat for storage, (4) holding genetic influences constant, body fat is closely adjusted to the amount of fat in the diet, and (5) considering that the body burns a blend of glucose and fat in its fuel mixture, perhaps the best way to lose weight is to eat less fat in your daily diet than the body burns in its fuel mix. Weight loss will be gradual and level off when the body makes a new adjustment in its fuel mix to match the change in diet. An additional benefit of lowering fat intake and increasing carbohydrates (in the form of more fruit, vegetables, and grain foods) is that total caloric intake tends to decrease automatically, facilitating weight loss. Because of the difference in caloric density (4 calories per gram of carbohydrate, 9 per gram of fat) and the much greater bulk of carbohydrate foods compared with fat due to their water, air and fiber content, one cannot easily consume as many calories on a high-carbohydrate diet as on a high-fat diet.

Whereas little or no carbohydrate is converted for fat storage with a short-term bout of carbohydrate overfeeding, and such overfeeding is met with an increase in metabolic rate, overfeeding with fat leads to immediate incorporation of the excess energy and no change in energy expenditure.⁵⁴ Approximately 97% of the energy contained in any overconsumption of dietary fat will be available for storage while a maximum of between 65 and

75 percent of the caloric content of carbohydrate will ultimately be available for storage, but only with prolonged overfeeding.⁵⁰

Finally, further work confirms the rebound elevation in AT-LPL after large amounts of weight loss and the continuing long-term influence of this enzyme in facilitating the regaining of weight, which was discussed earlier in this paper.⁵⁵ In addition, this recent work points to the activation of a gene inside fat cells that triggers the extreme elevation of AT-LPL. The fatter the person to begin with, and the more weight lost, the greater the elevation of AT-LPL, which seems to indicate that the more you lose, the harder your body will fight to regain its weight.

There is, however, considerable inconsistency in the research on the effects of dieting on AT-LPL. Studies that show the rebound elevation use massively obese subjects who follow very low calorie diets for prolonged periods of time. It is not clear whether the activity of this enzyme depends upon the initial weight of the person, the amount of previous overeating, the initial level of enzymatic activity, the degree of caloric restriction and speed of loss, the amount of weight lost, and the period of time during which a person follows any particular level of caloric restriction. There is some indication that a certain threshold of weight loss must be reached in the context of very low-calorie dieting before super-reactivity is triggered. It is also not clear whether the nutrient mixture of the diet can affect AT-LPL activity, that is, a low-fat diet without carbohydrate restriction versus various degrees of caloric restriction.

In conclusion, the two lines of research discussed above suggest that it is primarily the fat in the diet that leads to endogenous obesity and that the use of very low calorie diets by the massively obese for a prolonged period can have self-defeating aftereffects.

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