Environmental Contributions to the Obesity Epidemic

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The current epidemic of obesity is caused largely by an environment that promotes excessive food intake and discourages physical activity. Although humans have evolved excellent physiological mechanisms to defend against body weight loss, they have only weak physiological mechanisms to defend against body weight gain when food is abundant. Control of portion size, consumption of a diet low in fat and energy density, and regular physical activity are behaviors that protect against obesity, but it is becoming difficult to adopt and maintain these behaviors in the current environment. Because obesity is difficult to treat, public health efforts need to be directed toward prevention.

Obesity has reached epidemic proportions in the United States and is threatening to become a global epidemic (*1*). According to the classification scheme established by the World Health Organization (*1*), 54% of U.S. adults are overweight [a body mass index (BMI) $\geq$ 25 kg/m^2] and 22% are obese (BMI $\geq$ 30 kg/m^2) (*2*). The prevalence of overweight has risen dramatically over the past two decades, and if this trend persists, the entire U.S. adult population could be overweight within a few generations (*3*). This alarming increase is also present among the nation's youth; 25% of U.S. children are overweight or obese (*4*). Obesity represents a serious threat to health because it increases the risk of developing many chronic diseases, such as diabetes and cardiovascular disease (*5*).

What is causing the dramatic rise in overweight among the population? Although research advances have highlighted the importance of molecular genetic factors in determining individual susceptibility to obesity, the landmark discoveries of leptin, uncoupling proteins and neuropeptides involved in body weight regulation, cannot explain the obesity epidemic. Our genes have not changed substantially during the past two decades. The culprit is an environment which promotes behaviors that cause obesity. To stop and ultimately reverse the obesity epidemic, we must "cure" this environment.

What behaviors contribute to obesity, and how does the environment foster these behaviors? On the simplest level, obesity can arise only when energy intake exceeds energy expenditure. Our current environment is characterized by an essentially unlimited supply of convenient, relatively inexpensive, highly palatable, energy-dense foods, coupled with a lifestyle requiring only low levels of physical activity for subsistence. Such an environment promotes high energy intake and low energy expenditure. Under these circumstances, obesity occurs more frequently because, while the body has excellent physiological defenses against the depletion of body energy stores, it has weak defenses against the accumulation of excess energy stores when food is abundant.

An individual's body weight and body composition are determined by interactions between the environment and genetics (*6*). The environment's contribution to obesity must be thought of in terms of how it increases the frequency of behaviors that increase the risk of positive energy balance. With positive energy balance, body mass increases in order to restore energy balance. In this sense, obesity can be viewed not as a result of defective physiology, but as the natural response to the environment. Within any given environment, an individual's becoming obese is not a certainty, but an event that occurs with a certain probability. Some individuals can avoid obesity in unsupportive environments by maintaining a pattern of healthy behaviors. Genetic makeup also plays a role in that it determines the strength of an individual's physiological defense against gaining and maintaining an obese body fat level. Genetic factors are critically important for determining how different individuals respond within a given environment. This is best illustrated by the differences in body weight among individuals living in a common environment.

In a society in which food availability is not limited, weight maintenance, whether at normal or elevated body fat level, is accomplished primarily by the regulation of food intake (*7*). Small differences in metabolic efficiency between individuals, historically the focus of much research, are insufficient to explain the prevalence of obesity. For any given genotype, resting energy expenditure has only a limited capacity to adjust to changes in food intake in order to maintain energy balance. Even under extraordinary circumstances such as fasting or forced overfeeding, energy expenditure is changed by only 5 to 10% (*8*). Changes of this magnitude are insufficient to blunt the effects of large alterations in food intake on body weight and composition.

What Environmental Factors Promote Overeating?

Food availability and portion size. One way in which the current environment promotes obesity is by providing more frequent opportunities for the consumption of large quantities of food. A variety of highly palatable, inexpensive foods is available nearly everywhere. Compounding this is a growing trend in the United States toward larger portions. This is especially evident in so-called fast food restaurants, where "super sizing" of menu items is commonplace. Our culture's apparent obsession with "getting the best value" may underlie the increased offering and selection of larger portions and the attendant risk of obesity.

High-fat diets. The effects of diet composition on the development of obesity can be clearly seen in animal models. Obesity is rare in experimental animals maintained on a low-fat diet, even when they are housed in small cages that limit physical activity. In contrast, providing sedentary animals with ad libitum high-fat diets ($\geq$35% of energy from fat) reliably produces increases in energy intake, increases in efficiency of body fat gain, and obesity (*9*). For example, the average percent body fat of mice was found to increase in direct proportion to the percentage of energy as fat in the diet (*10*). Furthermore, although the overall prevalence of obesity increased as dietary fat increased, so did the variation in response between different animals fed the same level of dietary fat. At the highest levels of dietary fat, some animals became markedly obese, most gained significant amounts of body fat, and a few did not gain appreciable fat compared with control animals fed very low-fat diets.

Studies in humans also support a role for dietary fat in the development of obesity. In numerous studies, total energy intake was higher when subjects consumed diets rela-

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tively high in fat than when they ate lower fat diets (*11*). Although the primary impact of high-fat diets on obesity may be through effects on food intake, body fat storage also occurs at a greater rate when excess energy comes from fat than when it comes from carbohydrate or protein (*8*).

Behavioral factors can modulate the effect of dietary fat on the development of obesity. A recent report (*12*) described the results of a 6-month trial in which subjects came to a research "supermarket" to obtain either full-fat or reduced-fat foods. Subjects who selected full-fat foods had, on average, a higher energy intake and gained weight during the trial, whereas subjects selecting from reduced-fat foods did not increase energy intake or change body weight. Dietary restraint (a measure of the extent to which conscious control is exerted on food intake) provided protection against the obesity-promoting effect of the high-fat, high–energy density diet. Restrained eaters, as compared with unrestrained eaters, avoided increases in energy intake and weight gain on the full-fat diet and lost weight on the low-fat diet. This suggests that careful control of food intake can prevent weight gain on a high-fat diet. The advantage of the low-fat diet was that weight gain was avoided without the need for high levels of dietary restraint.

The apparent effect of fat per se on energy intake in these studies is difficult to separate from an effect of energy density. Subjects tended to eat a constant weight of food on both high- and low-fat diets. Because fat provides more energy per gram than other nutrients, high-fat foods have a higher energy density than low-fat foods. It is possible that the energy density of the diet rather than the dietary fat was responsible for the increased energy intake. This hypothesis is supported by studies which show that energy intake varies with energy density when dietary fat content is maintained at a constant level (*13*).

Practically speaking, the energy density of many foods, especially those with a caloric density above 3 to 4 kcal/g, varies directly with the percentage of fat in the foods. However, an increasing number of fat- and calorie-modified foods that are low in fat have an energy density that is as high as or higher (because of low fiber and water content) than that of either the foods they replaced or more traditional low-fat foods such as whole grains, fruits, and vegetables. Including these novel high-energy foods in the diet may not limit total energy intake as would occur when composing a diet from among more-traditional low-fat foods. Recognizing the importance of energy density is a step forward in understanding how food composition affects total energy intake, but reductions in dietary fat may still be the most effective means of reducing the likelihood of excessive energy consumption. Although not all energy-dense foods are high in fat, few high-fat foods are low in energy density.

The debate over dietary fat and obesity. Not all investigators agree that dietary fat promotes the development of obesity (*14*). Proponents of a counter viewpoint argue that obesity prevalence has increased whereas the percentage of energy intake from dietary fat has declined, and that reductions in dietary fat produce only modest reductions in body weight. While it is true that dietary surveys indicate that fat as a percentage of energy intake has declined from 37 to 34% over the past decade, fat intake in grams per day has remained essentially constant at 80 g/day over the same period (*15*). Further, some investigators have suggested that in the wake of public education to reduce fat intake, dietary fat intake may be underreported, so that the dietary fat estimates from these recent dietary surveys may be low.

The major impact of reducing dietary fat is likely not on reversing obesity but on preventing weight gain in the first place. Given the strength and redundancy of physiological mechanisms defending against weight loss, it is remarkable that reductions in dietary fat (without specifying reductions in total energy intake) have been uniformly associated with some, albeit modest, loss of body weight (*16*).

Laboratory studies in rodents and humans have consistently demonstrated the obesity-producing effects of high levels of dietary fat, but there are as yet no large prospective trials testing the hypothesis that reducing dietary fat and energy density can prevent obesity. This should be an important priority for future research.

What Environmental Factors Promote Physical Inactivity?

Low levels of physical activity are associated with an increased risk of obesity (*17*), and our current environment tends to discourage physical activity. Advances in technology and transportation have reduced the need for physical activity in daily life. The appeal of television, electronic games, and computers has increased the time spent in sedentary pursuits among children and adults alike. A large portion of our population already lives a sedentary life, and it is difficult to imagine that this trend will not continue in the future. A low level of physical activity is associated with a low daily energy requirement and will cause obesity unless food intake is limited accordingly.

Facilitating this trend is the fact that most children in the United States do not engage in daily physical activity at school. Cutbacks in mandatory physical education programs have contributed to overall declines in children's physical activity levels. Even when these programs are available, they are often taught by untrained individuals, involve little actual physical activity, and do not focus on the fun aspects of physical activity (*17*).

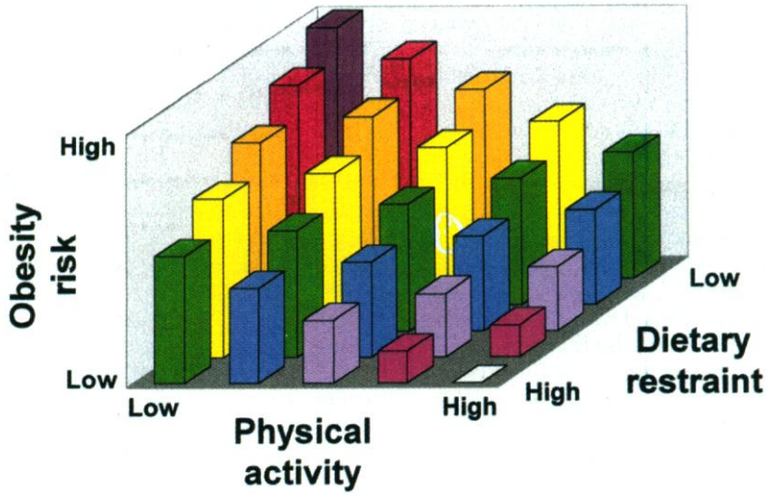

Fig. 1. Hypothetical risk of obesity in individuals consuming a diet high in energy density. This risk can be modified by physical activity and by conscious limitation of total energy intake (dietary restraint). As the energy density of the diet decreases, the risk of obesity (the height of all of the bars) would be expected to decline.

Interaction of Food Intake and Physical Activity

What do we really know about the interaction of food intake and physical activity

patterns? Will consumption of a low-fat, low–energy density diet prevent obesity in sedentary individuals, and will regular physical activity protect even those people eating a high fat, high–energy density diet? The answers to these questions seem obvious, but there is little direct empirical evidence to prove the effectiveness of these strategies. Clinical data, however, provide strong evidence that physical activity mitigates the effects of fat-rich diets on energy balance. In a series of studies, subjects were given ad libitum access to low-, medium-, and high-fat diets under sedentary or physically active conditions (*18*). At each level of dietary fat, the sedentary condition produced more positive energy balance than the active condition, highlighting the protective effect of physical activity. For each level of activity, higher dietary fat increased the degree of positive energy balance, highlighting the obesity-promoting effect of fat (energy density). Overall, energy balance under any condition was determined not by diet or activity alone, but by the interaction between the two.

Figure 1 shows the hypothetical risk of developing obesity in subjects eating a high–energy density diet (for example, a typical Western diet). These individuals can maintain a relatively low risk of obesity by engaging in high levels of physical activity, by high dietary restraint, or by a combination of moderate activity with some dietary restraint. For sedentary individuals, avoidance of positive energy balance and obesity will likely require a high level of dietary restraint or consumption of a diet low in energy density. Figure 1 illustrates what would happen with a high–energy density diet. As the energy density of the diet declines, the height of all of the bars in the figure should be reduced.

What Can We Do to Cure the Environment?

To combat the epidemic of obesity, we must first cure the environment. There are at least three major ways to promote behaviors that protect against obesity. One step would be a consumer education effort to reduce portion sizes, which may help to limit opportunities for "passive overeating." The food and restaurant industries should be encouraged to take responsible actions by reducing portion sizes, especially of high–energy density foods.

A second step would be to increase the availability of foods that are low in fat and low in energy density. Simply telling people to eat such diets will bring only limited success, given the current food supply. Foods that are naturally low in fat and energy density, such as fruits, vegetables, and whole grains, should be made easily available and affordable in both restaurants and grocery stores. The development of more low–energy density foods that taste as good as the high–energy density versions may also facilitate consumption of low–energy density diets.

We also need to foster a preference for less energy-dense foods in young children. We must learn more about how children's eating patterns develop and how they can be modified. Studies suggest that very young children are good regulators of energy intake (*19*), and that they can "unlearn" this regulation over time. Consistently asking a child to "clean your plate," for example, may accustom them to ignore or override physiological satiety cues.

Successful public health efforts in the area of diet may require collaboration among the agricultural and food industries (to provide appropriate foods), educators (to promote healthy choices), government (to provide incentives), and researchers (to investigate the mechanisms underlying the regulation of food intake).

A third major step would be to make the environment more conducive to physical activity. Increasing the physical activity level of the general population is an enormous challenge. Public health efforts could involve development of appropriate incentives. People who engage in regular physical activity generally have fewer health problems and fewer days absent from work than sedentary people. Active individuals could be rewarded with reduced insurance costs or additional vacation time, for example.

Schools should encourage children to engage in daily physical activity. Trained instructors should teach basic physical education skills and expose children to fun physical activities that set the stage for lifelong habits. There are critical research needs in this area. We need to understand more about the factors within the environment that affect physical activity patterns, how these patterns develop in children, and how they "track" into adulthood. We also need to investigate how much physical activity is required to prevent the development of obesity under different environmental circumstances and at different ages. We need to find creative ways to counter attractive sedentary pursuits. Children are more likely to participate in physical activity if the activity is fun and if parents also participate.

It is unlikely that we will reverse a sedentary lifestyle solely by promoting increased leisure time activity. We must also increase physical activity in the routines of daily life—for example, by occasionally using physical activity rather than meals as the focal point of family gatherings.

What Are the Barriers to Altering the Environment to Prevent Obesity?

Health professionals, the general public, and policy-makers have not recognized obesity as a serious threat to health. Despite overwhelming evidence about the consequences of obesity and clear indications that obesity has reached epidemic proportions, it remains low on the list of important public health problems.

A second barrier is the perception that we do not know how to prevent obesity. Evidence from the National Weight Control Registry (NWCR), which monitors individuals who have successfully maintained a weight reduction for at least 1 year, suggests that we can prevent weight gain by promoting the behavioral changes suggested above. These reduced-obese individuals (who have maintained an average weight loss of 67 pounds for an average of 5 years) are at high risk for weight gain. They report that their success in weight maintenance is due to consumption of a low-fat diet, low total energy intake, and high levels of regular physical activity (*20*). The failure of many people to avoid obesity may be due to a failure to adopt and maintain these behaviors in our current environment.

Altering the environment to encourage behaviors that prevent obesity may appear to be an insurmountable challenge. Changing the environment to reduce cigarette smoking must have seemed equally insurmountable in the 1960s, yet partnerships among educators, government, and industry have led to substantial reductions in the number of people who smoke. Currently, the rate of HIV infection is declining as a result of public health education that increased awareness of the specific behaviors that were leading to the spread of AIDS. Dealing with obesity may require a similar strategy. We must begin now to form the necessary partnerships to develop cost-effective strategies to stem the obesity epidemic. It may be decades before such efforts realize success, but the dramatic increase in obesity prevalence suggests that we are rapidly losing the opportunity to prevent this public health threat.

REFERENCES AND NOTES

1. World Health Organization, *Obesity: Preventing and Managing the Global Epidemic* (World Health Organization, Geneva, 1998).
2. K. M. Flegal, M. D. Carrol, R. J. Kuczmaraki, C. L.

Johnson, *Int. J. Obes.* **22**, 39 (1998).
3. J. P. Foreyt and G. K. Goodrick, *Lancet* **346**, 134 (1995).
4. R. P. Troiano and K. M. Flegal, *Pediatrics* **101**, 497 (1998).
5. F. X. Pi-Sunyer. *Ann. Intern. Med.* **119**, 655 (1993).
6. J. O. Hill, M. J. Pagliassotti, J. C. Peters, *Genetic Determinants of Obesity*, C. Bouchard, Ed. (CRC Press, Boca Raton, FL, 1994), pp. 35–48.
7. J. P. Flatt, *Diab. Rev.* **4**, 433 (1996).
8. T. J. Horton *et al.*, *Am. J. Clin. Nutr.* **62**, 19 (1995); M. E. J. Lean and W. P. T. James, *Int. J. Obes.* **12**, 15 (1988).
9. S. Chang *et al.*, *Am. J. Physiol.* **259**, R1096 (1990); A. Sclafani, *Ann. N.Y. Acad. Sci.* **575**, 281 (1989).
10. D. M. Salmon and J. P. Flatt, *Int. J. Obes.* **9**, 443 (1985).
11. L. Lissner, D. A. Levitsky, B. J. Strupp, H. J. Kalkwarf, D. A. Roe, *Am. J. Clin. Nutr.* **46**, 886 (1987); B. J. Rolls and V. A Hammer, *ibid.* **62**, 1086S (1995); R. J. Stubbs, P. Ritz, W. A. Coward, A. M. Prentice, *ibid.*, p. 330; B. J. Rolls and D. J. Shide, *Nutr. Rev.* **50**, 283 (1992).
12. M. S. Westerterp-Plantenga *et al.*, *Int. J. Obes.* **22**, 14 (1998).
13. R. J. Stubbs, C. G. Harbron, P. R. Murgatroyd, A. M. Prentice, *Am. J. Clin. Nutr.* **62**, 316 (1995).
14. E. A. Bell *et al.*, *ibid.* **67**, 412 (1998).
15. W. C. Willett, *ibid.*, p. 556S.
16. N. D. Ernst *et al.*, *J. Am. Diet. Assoc.* **97**, S47 (1997); A. Astrup, S. Toubro, A. Ruben, A. R. Skov, *ibid.*, p. S82.
17. U.S. Department of Health and Human Services, *Physical Activity and Health: A Report of the Surgeon General* (U.S. Department of Health and Human Services, Atlanta, GA, 1996).
18. R. J. Stubbs, *Nutr. Bull.* **19**, 53 (1994).
19. L. L. Birch, S. L. Johnson, G. Andersen, J. C. Peters, M. C. Schulte, *N. Engl. J. Med.* **324**, 232 (1991).
20. M. L. Klem, R. R. Wing, M. T. McGuire, H. M. Seagle, J. O. Hill, *Am. J. Clin. Nutr.* **66**, 239 (1997).
21. We thank A. Kriketos for help in preparing this manuscript. Supported by NIH grants DK42549, DK38088, and DK48520. Because of space limitations, it was not possible to include a comprehensive list of references for all of the work discussed. References (*1*) and (*6*) provide a more comprehensive reference list. The Procter and Gamble Company markets both regular and low-fat food products.

The Search for Human Obesity Genes

Anthony G. Comuzzie and David B. Allison

Understanding of the genetic influences on obesity has increased at a tremendous rate in recent years. By some estimates, 40 to 70 percent of the variation in obesity-related phenotypes in humans is heritable. Although several single-gene mutations have been shown to cause obesity in animal models, the situation in humans is considerably more complex. The most common forms of human obesity arise from the interactions of multiple genes, environmental factors, and behavior, and this complex etiology makes the search for obesity genes especially challenging. This article discusses the strategies currently being used to search for human obesity genes and recent promising results from these efforts.

One of the greatest challenges in biomedical research today is the elucidation of the underlying genetic architecture of complex phenotypes such as obesity. At first glance, body weight seems exceptionally simple. It can be defined precisely and measured with great accuracy and reliability. However, recent research on obesity has revealed that body weight is in fact a truly complex phenotype. As an amalgamation of literally everything we are physically, body weight is influenced by any factor that influences the weight of any individual tissue, organ, or fluid. Indeed, obesity may represent the archetype of the so-called "complex phenotypes." In contrast to simple Mendelian disorders, in which there is generally a one-to-one relationship between genotype at a single locus and the presence or absence of the disorder, obesity arises as a result of numerous behavioral, environmental, and genetic factors. The role of behavior and environment in the development of obesity is described elsewhere in this issue (*1*). Here, we discuss our current understanding of the genetics of human obesity, with an emphasis on some of the special challenges this complex condition poses to would-be gene finders.

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Genetic Approaches to Human Obesity

Although there is longstanding evidence that genetics plays an important role in the body weight of livestock and laboratory rodents, an appreciation of the genetic contribution to human obesity is a relatively recent development. Twin, adoption, and family studies have now established that an individual's risk of obesity is increased when he or she has relatives who are obese (*2*). Other studies have shown consistently that ~40 to 70% of the variation in obesity-related phenotypes, such as body mass index (BMI), sum of skinfold thickness, fat mass, and leptin levels, is heritable (*3*). Finally, numerous segregation analyses (studies evaluating the evidence and mode of transmission for a major gene based on observed patterns of phenotypic inheritance among related individuals) have provided evidence that among the genes that influence these obesity-related phenotypes, at least a few exert relatively large effects. In fact, anonymous major genes accounting for as much as 40% of the variation in BMI (*4*) and ~40% of the variation in fat mass (*5*) have been reported, along with major genes influencing specific measures of adipose tissue distribution (*6*). Importantly, some of these genes appear to exert their effects across various ethnic populations. While there will undoubtedly be rare obesity-predisposing alleles whose phenotypic effect is restricted to isolated populations or even families, the possible existence of at least a few common alleles with measurable effects on obesity has particularly important public health implications. It is these genes that may reveal new avenues for treatment and allow identification of at-risk individuals for the largest portion of the population.

Emphasis has shifted from the question of whether human obesity has a genetic component to which specific genes are responsible. Studies of animal models (*7*) have identified several genes with measurable effects on body weight and composition, supporting the concept that such genes exist. A key point of debate in the search for these genes is the optimal sampling strategy, both in terms of the unit of study (for example, sibling pairs versus extended families) and in the mode of ascertainment (for example, affected individuals versus randomly selected probands). Four sampling procedures are being used:

(i) Random or haphazard sampling, in which individuals are selected without regard to their phenotype or family structure. This method has the advantages of representativeness and convenience but offers low statistical power.

(ii) Sampling of large sibships or pedigrees. This method also allows analysis of individuals who are phenotypically representative of the population but offers higher statistical power than random sampling. Al-