

# A Clinical View of the Obesity Problem

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The increased rate of obesity in the past decade is caused by a larger rate of energy input than energy expenditure. But this simple explanation belies the complexity of the possible solutions: Education about obesity needs to improve for both the medical community and the public. Successful treatment will require reforms of medical practice as well as more research to facilitate the development of new drugs.

The worldwide problem of obesity is sparked by two factors: increased intake of food and increased sedentariness. The energy balance equation is a simple one: To maintain a steady body weight, energy in must equal energy out. It is difficult for people to control both their intake and their expenditure of energy. Intake has gone up because in the developed world food is now very abundant, very available, very palatable, and very cheap. At the same time that our buffet table is growing more luxurious year by year, physical activity is declining (1, 2). Both at work and at play, people do less and less physical exertion each year.

As the number of people who are obese increases, the number seeking care for their condition also rises and it has become dogma that treating obesity is ineffectual. This is not really the case, as I will endeavor to show below. But it is a certainty that treatment is very difficult. Why is this so? Although all the answers are certainly not in, a number of reasons for the difficulty both patients and their physicians encounter are evident.

The struggle for survival of the human species has been driven by a lack, not an excess, of food. Over the eons of human existence, famine has been a constant threat to the species. The human body has developed over the years to defend actively against this threat. As soon as weight is lost, there is a powerful biological drive to regain it. Basal metabolism (that is, energy expenditure) drops quite dramatically, and hunger signals leading to a powerful stimulus to search for and consume more food greatly increase (see the accompanying News story by J. Marx).

In contrast, when there is an accretion of excess weight, the biological signals for reversing this are very muted. There is no great increase in energy expenditure and there is no drive for greater physical activity; on the contrary, individuals tend to become more sedentary (3). In addition, food intake does not readily drop. Also, for reasons that are not clearly understood, people tend to defend the highest weight that they attain (4). The body protects body fat reserves at whatever level

they are, and when one loses from the reserves, powerful signals are generated for returning the reserves to the highest level attained. What is a wisdom of the body in times of deprivation becomes a foolishness in our modern environment. In the long run, I believe that the problem will be solved by two things: better education and better drugs.

## Education

What can be done to address the first item and bring what is known about nutrition and obesity into actual practice in the lives of Western people? The first requirement is better nutrition and counseling education for medical practitioners. Modern schools of medicine do almost nothing to train practitioners who are conversant and comfortable with treating people with obesity. As a result, these practitioners are very poorly equipped to give advice to their patients. There needs to be much stronger nutritional knowledge and more training in counseling skills that will allow them to be more effective in facilitating life-style changes in their patients.

Most important is a second requirement: education of the public at large. Although health education takes time, it ultimately can be a powerful means of changing population habits. We have seen this in the past two decades with regard to smoking. With solid evidence that smoking is deleterious to health, the campaign to educate the public has been gaining ground year by year. The evidence for the relationship between obesity and a whole host of chronic illnesses is also clear. Being obese predisposes to diabetes mellitus, coronary artery disease, stroke, sleep apnea, degenerative joint disease, and most likely certain forms of cancer (5). Because treatment is difficult, prevention is a much preferable route. I am sanguine that this is a viable option, because it is already proving effective in one segment of the population: those in the upper educational and economic brackets. The prevalence of obesity in these groups is remarkably lower than in other groups. They are by behavioral habits restrained eaters, despite the difficult environment in which they live. It is therefore clearly possible for people to remain at healthy weights in modern society. What it

requires is a consciousness of the problem; a motivation to remain lean; and appropriate tools, confidence, and self-image to sustain the effort through the years.

As people become more aware of the health dangers of obesity, they will be more apt to worry about it, will try to prevent it, and will try to combat it early in its course when it is more manageable and the chances of success are much higher. This is a difficult message to get across, however, because the initial development of overweight comes with few health side effects of a major kind. Only after a number of years of carrying an excess fat burden do the associated unhealthy conditions tend to occur. Although the risk factors are elevated early, symptoms are not. Vigorous and creative campaigns will be necessary to raise public consciousness of the problem as a health issue.

## Treatment

Although prevention is clearly the best way to try to solve this health problem, treatment can be successful once obesity has occurred and should not be ignored. There have been numerous reports of the successful loss of body weight (6, 7). Behavior modification focused strictly on nutrition and activity change can be successful in large as well as small studies (8, 9). The focus is on life-style changes that are realistic and doable (10). Because risk factors for chronic disease that are associated with obesity tend to improve with even modest weight loss (11, 12), a reasonable goal is not to try to reach normal weight but to aim to lose 10% of the starting weight. Such a goal can be reached with appropriate education and support, and it can be maintained over time in individuals who have changed their life-style so as to eat a healthy diet and be physically active (13).

There are several requirements for improving obesity treatment. The first is more time—more time for health practitioners to interact with their patients. It is difficult for practitioners to help their patients lose weight or maintain weight loss when they can allocate only 12 to 15 min per patient and see the patient only three to four times per year. Intervention requires persistence and repeated contact and takes a significant amount of time. This necessary time is missing from the treatment paradigm. Another approach, not used widely enough, is to train other health professionals (such as dietitians, exercise physiologists, nurses, and psychologists) to provide treatment. Such professionals have

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been remarkably successful in various trials (8, 9) and have the time and interest and can acquire the skills to make them excellent practitioners in this area.

The second requirement is reimbursement for treatment of obesity. As long as third-party payers do not reimburse for obesity treatment, there will be little interest on the part of the medical profession in treating it. This has become a catch-22. Third-party payers do not want to pay for treatments that are not guaranteed to produce effective outcomes, but effective outcomes do not occur because practitioners cannot spend enough time engaged in producing effective outcomes. How to break this vicious cycle is not clear.

The third requirement is better drugs. As we learn more about the mechanisms underlying food intake regulation and energy expenditure, we will be able to intervene more effectively to decrease the former and increase the latter. We need an armamentarium of safe and effective drugs. The history of weight-loss drugs is strewn with ones that have not been safe, from amphetamines to phentermine-fenfluramine, and their efficacy has generally been low. As the molecular signals that regulate food intake and energy expenditure are better characterized, we are likely to get better, safer, and more diverse medications (see the accompanying News story by T. Gura).

Finally, it is clear to me that we need much more research. The investigation into this disease requires a multipronged effort. I suggest a few areas where clarification could be of great benefit. First, there is the genetic influence on food intake and energy expenditure. We need to learn more about which genes are important in turning food intake on and off and influencing energy expenditure. With this knowledge, we can identify the peptides and other molecules involved in these processes and begin to target possible pharmacological solutions to the issue. The second is to begin to look seriously at the

genetic underpinnings of behavior. Physical activity is behavior, and we have little idea what genes are important in making some people feel a need or an interest in being more active. More investigation in this area could have a large payoff, again in terms of possible pharmaceutical targets. Third, we need a great deal more knowledge about the fat cell as an endocrine organ. It is now clear that fat cells secrete a number of substances that can have a profound effect on weight and also on the comorbidities of obesity. In addition, all fat depots are not similar, and fat cells in different depots secrete a differing array of substances. The cataloging and investigating of these differences and understanding how they come about would greatly clarify the role of the fat cell in human disease. Fourth, we need to explore further the differing role of fat in health risk at various sites. New knowledge about the effects of deposition of fat in aberrant sites, such as skeletal muscle, the liver, and the beta cells of the pancreas is also needed. At these important sites, fat deposits are detrimental to health, but it is not clear how. Fifth, we need more information on circulating fat and how it interacts with the use of fuels in the body. We need to investigate not only the role of free fatty acids but also of specific fatty acids that may well have quite different effects on carbohydrate and fat utilization. Sixth, more work needs to be done on the relationship of obesity to inflammation. Obese people display evidence that their bodies respond to one or more inflammatory stimuli. What these are and how they work in promoting disease is very unclear. It is an important issue, because inflammation is also involved in the progression of some of obesity's comorbidities, such as diabetes, atherosclerosis, coronary artery disease, and stroke. Seventh, we need better, longer, and more comprehensive studies of different diets and their benefits and risks. It is surprising that it has been so difficult to get granting agencies to fund such studies.

Both practitioners and the public are clamoring for more information. What about a high-fat diet versus a high-protein diet versus a high-carbohydrate diet? There have not been any large enough, long enough studies that have explored the benefits, risks, compliance, dropout rates, and quality of life produced by varying diets. These should certainly be done. Finally, possibly related to dietary studies, we need to focus more on the risks of weight loss. Weight loss once weight gain has occurred may not be good for the body. Although there is controversy on this point, we need more data on the risks and benefits of weight loss once obesity has supervened. This is an interesting and underinvestigated field crying out for more data.

Weight loss is difficult but possible to attain. Weight maintenance is harder but also possible. Our tools for tackling the rapidly increasing public health problem of obesity are weak because our knowledge base is still remarkably low. As we learn more about the basic biology of the regulation of body weight, food intake, and energy expenditure, our attempts at interventions should greatly improve.

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