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Sylvia R. Karasu M.D.
The Gravity of Weight

"Did You Ever See a Fat Squirrel?"

Not why are many overweight, but why is anyone thin?

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Our bodies process about a million calories each year. That's ten million calories in a decade. Given the typical environment in which most of us find ourselves, with an overwhelming array of caloric possibilities, "Why is anyone thin?" So asked Dr. Jeffrey Friedman, one of this year's recipients of the Lasker Award (often called the "American Nobel.") In other words, perhaps we shouldn't always be asking why there are so many overweight or obese people, but rather instead, given our environmental temptations, we should be asking how anyone remains at a normal weight. In an article in the *American Journal of Clinical Nutrition* from last year, Friedman acknowledged that the obese eat too much and exercise too little. For the most part, it is the First Law of Thermodynamics-that is, essentially, calories in, calories expended. The "deeper question" for Friedman, though, is why do the obese eat more and exercise less. And his answer is that it is sometimes "less about conscious choices" and "more about their biological makeup." To a large extent, this is determined by our genetics.

Some people, no matter how little they eat or how much they exercise, will always have a weight problem; conversely, others, no matter what they do, will never gain much weight. And our bodies have evolved to preserve the status quo, or in biological parlance, homeostasis. So when we lose weight, our bodies are

predisposed to regain the weight and conserve energy. And anecdotally, it seems the more rapidly we tend to lose the weight, as, for example, with severe calorie restriction, the more rapidly our bodies tend to regain.

***"D**id You Ever See a Fat Squirrel?"* was the title of a popular diet book by Ruth Adams in the early 1970s. Perhaps not a fat squirrel, but have you ever seen an obese mouse, which has a genetic mutation that leads to a leptin deficiency, massive obesity, excessive overeating (hyperphagia), insulin resistance, and other metabolic abnormalities? An obese mouse with this genetic mutation is in the photo above, with a normal mouse for comparison. In the early 1990s, it was Friedman's laboratory at New York City's Rockefeller University that first isolated the hormone leptin, found predominantly in fat tissue and one of the hormones responsible for regulating food intake and energy balance, among its many other functions. An actual genetic leptin deficiency is quite rare in humans, which is unfortunate, since giving exogenous leptin can reverse the obesity and the accompanying metabolic abnormalities in these people. Would that the genetics were that simple! In fact, most obese people have a state of excessive, but ineffective leptin, analogous to the state of insulin resistance. Giving injections of leptin, in general, never became the panacea weight loss solution originally anticipated, though leptin may eventually have more of a role in preventing weight gain, particularly in combination with other medications.

The obese mouse, with normal weight mouse for comparison

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We know from family, twin, and adoption studies that about 70% (and estimates up to 90%!) of our weight is genetically determined and perhaps as hereditable as our height. Actually, some researchers believe weight is more hereditable than most other conditions, including heart disease, breast cancer, hypertension, or even mental illness. Many years ago, Claude Bouchard and his colleagues did some classic experiments on a metabolic unit in which different sets of identical twins were exposed to the same number of calories and same amount of exercise. The twin pairs themselves each gained about the same amount of weight, but, surprisingly, there were considerable differences in the weight gain among different pairs despite exposure to the same environment. Recently, Bouchard has emphasized that genetic variation "has much to do with the risk of becoming obese," even though it is clearly not the only cause.

In fact, though, genetics seems to determine even where our fat accumulates (e.g. whether around our abdomens-the so-called "apples" or around our thighs-the so-called "pears"), how we will respond to medications for weight loss, or even our reluctance to exercise (e.g. from differences in motivation and reward to differences in ability and coordination.) But we are not just talking about a few genes. Researchers studying the Human Obesity Gene Map found that there are over 300 separate trait areas (loci) that may be involved in weight control. Warden and Fisler, in a recent article in Progress in Molecular Biology and Translational Science, acknowledge the extraordinarily complex issues involved in the genetics of obesity. They believe, however, that an individual's genetic profile could eventually lead to greater "flexibility" in national recommendations for changes in lifestyle involving diet and exercise that are geared to preventing obesity. Even the USDA food pyramid and children's lunchboxes might be genetically individualized some day!

The point is that we can make our environment work with our genetics when it comes to weight control. So when you sit down to your Thanksgiving table this week, remember your genetic predispositions may weigh quite heavily, as it were, on you. But don't despair: The more you can appreciate and acknowledge the contribution of your biological makeup, the more you should be able to control your penchant to overindulge.

About the Author

Sylvia R. Karasu, M.D., is a clinical professor of psychiatry at Weill Cornell Medical College and the senior author of *The Gravity of Weight.*

In Print: *The Gravity of Weight: A Clinical Guide to Weight Loss and Maintenance*

Online: my own website