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The Real Cause of Obesity

It's not gluttony. It's genetics. Why our moralizing misses the point.

By **Jeffrey Friedman** | Newsweek Web Exclusive
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Despite receiving a MacArthur genius award for her work in Alabama "forging an inspiring model of compassionate and effective medical care in one of the most underserved regions of the United States," Regina Benjamin's qualifications to be surgeon general have been questioned. Why? She is overweight. "It tends to undermine her credibility," Dr. Marcia Angell, former editor of The New England Journal of Medicine, said in an interview with ABC News. "I do think at a time when a lot of public-health concern is about the national epidemic of obesity, having a surgeon general who is noticeably overweight raises questions in people's minds."

It is not enough, it seems, that the obese must suffer the medical consequences of their weight, consequences that include diabetes, heart disease, and cancer, and that cause nearly 300,000 deaths in the United States each year. They must also suffer the opprobrium heaped on them by people like Angell or Rep. James Sensenbrenner (R-WI), who advised the obese to "Look in the mirror because you are the one to blame." In our society, perhaps no group is more stigmatized than the obese.

The abuse is nothing new, of course. Four hundred years ago, Shakespeare had Prince Hal hurl a barrage of insults at Falstaff, calling him "fat-witted," "horseback-breaker," and a "huge hill of flesh." But Shakespeare had an excuse. In his time essentially nothing was known about the real reasons that people are fat. Today we have no such excuse. Modern medical science has gone a long way toward explaining the causes of obesity, and the bottom line is clear: obesity is not a personal choice. The obese are so primarily as a result of their genes.

Genetic studies have shown that the particular set of weight-regulating genes that a person has is by far the most important factor in determining how much that person will weigh. The heritability of obesity—a measure of how much obesity is due to genes versus other factors—is about the same as the heritability of height. It's even greater than that for many conditions that people accept as having a genetic basis, including heart disease, breast cancer, and schizophrenia. As nutrition has improved over the past 200 years, Americans have gotten much taller on average, but it is still the genes that determine who is tall or short today. The same is true for weight. Although our high-calorie, sedentary lifestyle contributes to the approximately 10-pound average weight

gain of Americans compared to the recent past, some people are more severely affected by this lifestyle than others. That's because they have inherited genes that increase their predisposition for accumulating body fat. Our modern lifestyle is thus a necessary, but not a sufficient, condition for the high prevalence of obesity in our population.

Over the past decade, scientists have identified many of the genes that regulate body weight and have proved that in some instances, different variants of these genes can lead a person to be fat or thin. These genes underlie a weight-regulating system that is remarkably precise. The average person takes in a million or more calories per year, maintaining within a narrow range over the course of decades. This implies that the body balances calorie consumption with calorie expenditure, and does with a precision greater than 99.5 percent. Even the most vigilant calorie counter couldn't compete, if for no other reason than that the calorie counts on food labels are often off by 10 percent or more.

The genes that control food intake and metabolism act to keep weight in a stable range by creating a biological force that resists weight change in either direction. When weight is gained, hunger is reduced. When weight is lost, the unconscious drive to eat is stimulated and acts to return weight to the starting point. Moreover, the greater the amount of weight that is lost, the greater the sense of hunger that develops. Thus, when the obese lose large amounts of weight by conscious effort, their bodies fight back even more strongly by increasing hunger and reducing energy expenditure. If you think it is hard to lose 10 to 20 pounds (and it is), try to imagine what it would feel like to lose many tens or even hundreds of pounds.

Anyone who doubts the power of this biologic system should study the case of a young boy in England a few years back. He had a mutation in a critical gene, the one that produces the hormone leptin. Leptin is made by fat tissue and sends a signal informing the brain that there are adequate stores of energy. When leptin drops, appetite increases. Because of a genetic error, this boy could not make this hormone, which left him ravenously hungry all of the time. At age 4 he ate 1,125 calories at a single meal—about half of what a normal adult eats in an entire day. As a result he already weighed 90 pounds and was well on his way to developing diabetes. At the time, his similarly affected cousin was 8 and weighed 200 pounds. After a few leptin injections, the boy's calorie intake dropped to 180 calories per meal, and by the time he was 6 his weight had dropped into the normal range. Nothing changed except the hormone levels: his parents weren't more or less permissive, his snacks did not switch from processed to organic, his willpower was not bolstered. Rather this boy was a victim of a malfunctioning weight-regulating system that led to an uncontrollable drive to eat. This examples illustrates that feeding behavior is a basic drive, similar to thirst and other life-sustaining drives. The key role of leptin and other molecules to control feeding behavior undercuts the common misconception that food intake is largely under voluntary control.

While mutations in the leptin gene like the cases described above are rare, nearly 10 percent of morbidly obese individuals carry defects in genes that regulate food intake, metabolism, and body weight. The evidence further indicates that the rest of the obese population carries genetic alterations in other, as yet unidentified, single genes or combinations of genes (polygenes) interacting with environmental factors.

So if you are thin, it might be more appropriate for you to thank your own "lean" genes and refrain from stigmatizing the obese. A broad acceptance of the biologic basis of obesity would not only be fair and

right, but would also allow us to collectively focus on what is most important—one's health rather than one's weight. There is no evidence that obese individuals need to "normalize" their weight to reap health benefits. In fact, it is not even clear whether there are enduring health benefits to weight loss among obese individuals who do not suffer from diabetes, heart disease, hypertension, or liver disease. What is known is that the obese who do suffer from these conditions receive a disproportionately large benefit from even modest weight loss, which together with exercise and a heart-healthy diet can go a long way toward improving health.

While research into the biologic system that controls weight is moving toward the development of effective therapies for obesity, we are not there yet. In the meantime we must change our attitudes toward the obese and focus less on appearance and more on health. In their efforts to lose weight they are fighting against their biology. But they also are fighting against a society that wrongly believes that obesity is a personal failing.

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