

Some people store fat and still avoid the harmful complications of obesity

October 7 2014, by Michael Blanding

What if you could gain as much weight as you wanted and remain relatively healthy? For a small percentage of people, that scenario isn't far-fetched.

We tend to think that obesity and poor health are constant companions. Indeed, studies have shown that being extremely overweight tends to lead to a host of medical problems, including heart disease, stroke and type 2 diabetes, which develop due to long-term adverse effects on the body's metabolism.

As doctors have looked at the causes and effects of obesity, however, they've begun to notice something strange. Not everyone who is obese develops those metabolic diseases associated with obesity. In fact, a small subset of the population with a [body mass index](#) above 30 (the definition of obesity) seem to live normal, healthy lives compared with the majority of [obese people](#).

"These people, called the metabolically healthy obese (MHO), are as fat as people who develop complications of obesity, yet they are protected from these complications," says Martin Obin, an adjunct scientist in the Nutrition and Genomics Laboratory at the Jean Mayer USDA Human Nutrition Research Center on Aging and an associate professor at the Friedman School. "Determining why MHO individuals are protected is going to tell us a great deal about how obesity causes chronic health problems."

Obin and Gerald Denis, an associate professor of pharmacology and medicine at the Boston University School of Medicine, explored this phenomenon in a paper, "Metabolically Healthy Obesity: Origins and Implications," published in the journal *Molecular Aspects of Medicine*.

The key, says Obin, seems to be in the way [fat cells](#) function in these metabolically healthy obese people.

Much of our body fat is contained in [white adipose tissue](#) (WAT), which stores excess energy as triglycerides in individual fat cells known as [adipocytes](#). Triglycerides are released during times of need, such as starvation or during exercise. WAT can store more triglycerides by increasing the number or size of the adipocytes, Obin says. In obese people, "adipocytes become excessively large, and their metabolism and function become dysregulated."

Inflammation Damage

When adipocytes get too large, they can become inflamed, causing them to secrete fatty acids that can lead to resistance to insulin (the hormone the body uses to dispose of excess sugar), a precursor to diabetes.

"If you are a marathon runner, you can pack in the pasta meals and not become fat, because you are burning it," explains Denis. "Otherwise, all those excess calories have to go somewhere. If the capacity of your adipocytes is exceeded, that puts stress on cells, some of which start dying, and that causes the inflammation."

By contrast, a small portion of obese people have WAT that can store high amounts of fat without causing the adipocytes to become huge—and these folks don't develop insulin resistance. "The result is that obesity in these individuals occurs with much less metabolic pathology," Obin says, noting that the "reasons for this important difference are

currently under intense investigation."

On the other side of the equation, some individuals, mostly women, suffer from the unhealthy [metabolic diseases](#) typically seen in obesity, even though they are of normal weight. Call them "skinny but unhealthy." Many of these women have the hormonal disorder polycystic ovary syndrome, which affects up to 10 percent of women. Even though half of women with the disorder are lean or even underweight, they still have higher secretions of fatty acids and insulin resistance.

The leading hypothesis to explain this key difference seems to be the way that white adipose tissue is distributed inside the body. Metabolically healthy obese people seem to have more WAT stored just beneath the skin rather than inside the body cavity. In addition, these individuals appear to have smaller adipocytes overall—meaning that when they get fatter, they create more adipocytes instead of their existing adipocytes getting bigger. That could lead to less inflammation.

Increased physical activity also seems to hold the most dangerous effects of obesity at bay.

That's why linebackers and sumo wrestlers can grow to enormous sizes that would be fatal in more sedentary people. "Sumo wrestlers are huge, but they are very healthy," says Denis. "Their blood profiles look great, and they have excellent glucose tolerance."

Keep Moving

Unfortunately, the beneficial effects seem to disappear as soon as the physical activity stops. "To retire from being a sumo wrestler is a death sentence," Denis says. "They are usually dead within a year, and so there is some urgency to develop safe ways to retire from professional sports where a high BMI is a normal requirement for a player."

Studies in genetically modified mice have shown specific genetic pathways that seem to determine these differences in WAT. One strain of transgenic mice, for example, produces increased levels of adiponectin, an anti-inflammatory protein secreted from adipocytes.

These mice display all of the features of metabolically healthy obese humans, including subcutaneous fat, smaller adipocytes and less inflammation. Obin and others have worked to knock out specific genes in order to reproduce this effect in other strains of mice, leading to increased secretion of adiponectin and other beneficial proteins and/or cutting down on inflammatory agents to produce healthier mice overall.

"I am surprised by the robustness with which abrogation of individual genes can uncouple adiposity from obesity complications, thereby generating fatter but fitter mice," Obin says.

Currently, researchers are studying these genetic models to see if they can be translated to therapies to treat obesity in humans. "It's not known whether it's possible to convert from metabolically unhealthy to healthy without losing weight," says Denis. The holy grail would be to create a pill that could recreate this cascade of beneficial factors to keep fat cells healthy and reduce [obesity](#)'s most harmful effects.

That wouldn't rule out the need for exercise, however. Obesity causes other complications, such as back problems, for which there is no metabolic fix. But it could go a long way toward improving the quality of life for obese people and minimizing health-care costs.

More information: "Metabolically healthy obesity': origins and implications." *Mol Aspects Med.* 2013 Feb;34(1):59-70. [DOI: 10.1016/j.mam.2012.10.004](#). Epub 2012 Oct 13. www.ncbi.nlm.nih.gov/pubmed/23068072

Provided by Tufts University

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