Overeating can set stage for obesity, researchers say

November 27 2009, By Sandi Doughton

It doesn't seem like a fair fight. In one corner loomed the Thanksgiving table, groaning with poultry, pie and mashed potatoes.

Cowering in the other corner: you, and your hope for a waistline smaller than your hips.

But as you wade into the battle of the holiday bulge, know that you are not unarmed.

The human body is equipped with an array of defenses to fend off fat, from ratcheting up metabolism to dialing down appetite.

In a lucky third of Americans, those tweaks are enough to maintain a remarkably stable body weight throughout a lifetime of dietary ups and downs.

But in a world where fast food beckons and calories have never come so cheap, the defenses can crumble for the rest of us. Figuring out why is one of the hottest topics in obesity research.

"That is literally the billion-dollar question," said Dr. Daniel Marks, director of Oregon Health & Science University's Child Health Research Center.

Scientists have long noted humans evolved in an environment where food was scarce. We're burdened by a biology that favors gorging and

packing on the pounds even though food is now plentiful for most of us.

Everyone agrees that powerful, internal forces conspire to make it hard to lose weight. But Marks is part of a growing cadre of researchers who also focus on the flip side of that equation: the fact that evolution gave us mechanisms -- albeit weak ones -- to prevent weight gain and protect against its harmful effects.

Too much fat would have made it hard for humans' ancient ancestors to escape predators and swing through treetops, said Dr. Michael Schwartz, director of the Diabetes and Obesity Center of Excellence at the University of Washington.

Recent studies suggest an overload of fat and nutrients is also dangerous at the cellular level, where it appears to trigger the inflammation that may set the stage for obesity.

BODY LIKES STATUS QUO

Researchers have a pretty good handle on the way defenses against weight gain are supposed to work, Schwartz said. The body's goal is to maintain the status quo, which it tries to do through chemical signals and directions from the brain.

One of the key controllers is a hormone called leptin, produced by fat itself.

When you gain fat, your leptin levels rise and alert your brain the status quo has been upset. The brain's normal response is to crank up metabolism and burn fat. Some people can even feel the heat after a particularly heavy meal, Schwartz said.

"They wake up in the middle of the night sweating. Your body is saying:

'You've eaten too much. We're going to burn it off.'"

The body also dampens appetite in response to weight gain, so that you feel full and stop eating sooner.

The changes in appetite and metabolic rate can persist for months or more, until the extra fat is gone, Schwartz said.

Experiments in the 1960s with prisoners fed massive amounts of food for six months found that most eventually dropped back to their original weights, said UW obesity researcher Dr. Greg Morton.

Even more dramatic are the Massa people of Cameroon, whose men can gain 60 pounds during two months of ritual fattening, Marks said. Researchers measured a 40 percent increase in the men's metabolic rates and found most lost the extra weight within a year.

Clearly, some individuals are better at fending off weight gain than others.

Faced with unlimited food, some rodent strains won't gain a gram, while some balloon into butterballs, Schwartz said.

If two people pig out during the holiday season and gain a couple of pounds, one may shed the extra weight effortlessly, while the other gains a lifelong paunch.

"Genetic factors affect susceptibility to a changing environment," Schwartz said. And the human environment has indeed been changing, as people exercise less and are presented nonstop with fattening food.

The result for many people is a slow, upward creep in weight.

The body still tries to maintain the status quo, but the baseline is higher.

"We sort of drift up over a long period of time, and our body gradually readjusts to our new weight," Marks said.

Once the body adjusts to a heavier status quo, it's hard to slim down again. When dieters lose fat, leptin levels drop, metabolism slows, appetite revs up -- and the weight usually roars back.

"Your brain ... thinks you're starving to death," said Rudolph Leibel, an obesity expert at Columbia University.

That drive to hold tight to your fat stores is more hard-wired -- and harder to disrupt -- than the system that defends against weight gain, Leibel said.

When weight-gain defenses do break down, the problem is rooted in the brain's sensitivity to leptin, Schwartz said. As fat stores increase and leptin levels rise, the brain becomes more and more impervious to the hormone's calls to put the brakes on weight gain.

Scientists are just starting to figure out why.

It turns out cells don't like to be "overfed," Schwartz said.

Faced with a heavy load of nutrients and fat, cells respond as if being attacked. They activate the same kind of inflammatory response that fights infection.

But when that inflammation hits the hypothalamus, the part of the brain that controls appetite and weight, it blunts the neurons' response to leptin.

"At the cellular level, the body does its best to process these huge influxes of calories, but when the system gets overwhelmed you begin to produce all kinds of toxic spinoff products that become the fuel for the fire that is obesity," Marks said.

Morton and Schwartz are exploring ways to restore leptin sensitivity, which holds out hope for future fat-fighting treatments.

Leibel cautions that the evidence doesn't yet nail inflammation as the cause of obesity. But he's optimistic researchers will eventually develop drugs that can at least help people who lose weight to keep it off.

In the meantime, is there anything a holiday eater can do to boost the body's defenses against weight gain?

Not much, the scientists concede. Marks advocates a diet rich in the omega-3 fatty acids found in fish, which can fight inflammation. He also suggests nibbling on hors d'oeuvres, eating slowly and waiting 30 minutes before dishing up that second helping. That gives your body enough time to send and receive the signals that say "I'm full."

Leibel's advice is not to let worries about weight spoil your Thanksgiving .

"Nobody ever got obese from a single meal," he said. "It's the other 364 days you need to pay attention to."

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