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A new way to lose weight? Study shows that changes to gut microbiota may play role in weight loss

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Scientists at Harvard may have new hope for anyone who's tried to fight the battle of the bulge. New research, conducted in collaboration with researchers at Massachusetts General Hospital, has found that the gut microbes of mice undergo drastic changes following gastric bypass surgery. Transfer of these microbes into sterile mice resulted in rapid weight loss. The study is described in a March 27 paper in *Science Translational Medicine*.

"Simply by colonizing mice with the altered microbial community, the mice were able to maintain a lower body fat, and lose weight – about 20% as much as they would if they underwent surgery," said Peter Turnbaugh, a Bauer Fellow at Harvard's Faculty of Arts and Sciences (FAS) Center for Systems Biology, and one of two senior authors of the paper.

But as striking as those results were, they weren't as dramatic as they might have been.

"In some ways we were biasing the results against weight loss," Turnbaugh said, explaining that the mice used in the study hadn't been given a high-fat, high-sugar diet to increase their weight beforehand. "The question is whether we might have seen a stronger effect if they were on a different diet."

"Our study suggests that the specific effects of gastric bypass on the microbiota contribute to its ability to cause weight loss and that finding ways to manipulate microbial populations to mimic those effects could become a valuable new tool to address obesity," said Lee Kaplan, director of the Obesity, Metabolism and Nutrition Institute at MGH and the other senior author of the paper.

"We need to learn a good deal more about the mechanisms by which a microbial population changed by gastric bypass exert its effects, and then we need to learn if we can produce these effects – either the microbial changes or the associated metabolic changes – without surgery," Kaplan, an associate professor of Medicine at Harvard Medical School, added. "The ability to achieve even some of these effects without surgery would give us an entirely new way to treat the critical problem of obesity, one that could help patients unable or unwilling to have surgery."

While the results were exciting, Turnbaugh warned that it may be years before they could be replicated in humans, and that such microbial changes shouldn't be viewed as a way to lose those stubborn last 10 pounds without going to the gym. Rather, the technique may one day offer hope to dangerously obese people who want to lose weight without going through the trauma of surgery.

"It may not be that we will have a magic pill that will work for everyone who's slightly overweight," he said. "But if we can, at a minimum, provide some alternative to gastric bypass surgery that produces similar effects, it would be a major advance."

While there had been hints that the microbes in the gut might change after bypass surgery, the speed and extent of the change came as a surprise to the research team.

In earlier experiments, researchers had shown that the guts of both lean and obese mice are populated by varying amounts of two types of bacteria, Firmicutes and Bacteroidetes. When mice undergo gastric bypass surgery, however, it "resets the whole picture," Turnbaugh said.

"The post-bypass community was dominated by Proteobacteria and Proteobacteria, and had relatively low levels of Firmicutes," he said. What's more, Turnbaugh said, those changes occurred within a week of the surgery, and weren't short-lived – the altered gut microbial community remained stable for months afterward.

While the results may hold out the hope for weight loss without surgery, both Turnbaugh and Kaplan warned that future studies are needed to understand exactly what is behind the weight loss seen in mice.

"A major gap in our knowledge is the underlying mechanism linking microbes to weight loss," Turnbaugh said. "There were certain microbes that we found at higher abundance after surgery, so we think those are good targets for beginning to understand what's taking place."

In fact, Turnbaugh said, the answer may not be the specific types of microbes, but a by-product they excrete.

In addition to changes in the microbes found in the gut, researchers found changes in the concentration of certain short-chain fatty acids. Other studies, Turnbaugh said, have suggested that those molecules may be critical in signaling to the host to speed up metabolism, or not to store excess calories as fat.

Going forward, Turnbaugh and Kaplan hope to continue to explore those questions.

"We think such studies will allow us to understand how host/microbial

interactions in general can influence the outcome of a given diet," Kaplan said. "To some degree, what we're learning is a comfort for people who have an issue with their weight, because more and more we're learning that the story is more complicated than just how much you exercise and how much you eat."

Provided by Harvard University