

Keto diet works best in small doses, researchers find

January 24 2020, by Brita Belli



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A ketogenic diet—which provides 99 percent of calories from fat and protein and only 1 percent from carbohydrates—produces health benefits in the short term, but negative effects after about a week, Yale researchers found in a study of mice.

The results offer early indications that the [keto diet](#) could, over limited time periods, improve [human health](#) by lowering diabetes risk and inflammation. They also represent an important first step toward possible clinical trials in humans.

The keto [diet](#) has become increasingly popular as celebrities, including Gwyneth Paltrow, Lebron James, and Kim Kardashian, have touted it as a weight-loss regimen.

In the Yale study, published in the Jan. 20 issue of *Nature Metabolism*, researchers found that the positive and [negative effects](#) of the diet both relate to [immune cells](#) called gamma delta T-cells, tissue-protective cells that lower diabetes risk and inflammation.

A keto diet tricks the [body](#) into burning fat, said lead author Vishwa Deep Dixit of the Yale School of Medicine. When the body's glucose level is reduced due to the diet's low carbohydrate content, the body acts as if it is in a starvation state—although it is not—and begins burning fats instead of carbohydrates. This process in turn yields chemicals called ketone bodies as an alternative source of fuel. When the body burns [ketone bodies](#), tissue-protective gamma delta T-cells expand throughout the body.

This reduces diabetes risk and inflammation, and improves the body's metabolism, said Dixit, the Waldemar Von Zedtwitz Professor of Comparative Medicine and of Immunobiology. After a week on the keto diet, he said, mice show a reduction in blood sugar levels and inflammation.

But when the body is in this "starving-not-starving" mode, fat storage is also happening simultaneously with fat breakdown, the researchers found. When mice continue to eat the high-fat, low-carb diet beyond one week, Dixit said, they consume more fat than they can burn, and develop

diabetes and obesity.

"They lose the protective gamma delta T-cells in the fat," he said.

Long-term clinical studies in humans are still necessary to validate the anecdotal claims of keto's health benefits.

"Before such a diet can be prescribed, a large clinical trial in controlled conditions is necessary to understand the mechanism behind metabolic and immunological benefits or any potential harm to individuals who are overweight and pre-diabetic," Dixit said.

There are good reasons to pursue further study: According to the Centers for Disease Control, approximately 84 million American adults—or more than one out of three—have prediabetes (increased blood sugar levels), putting them at higher risk of developing type 2 diabetes, heart disease, and stroke. More than 90 percent of people with this condition don't know they have it.

"Obesity and type 2 diabetes are lifestyle diseases," Dixit said. "Diet allows people a way to be in control."

With the latest findings, researchers now better understand the mechanisms at work in bodies sustained on the keto diet, and why the diet may bring health benefits over limited time periods.

"Our findings highlight the interplay between metabolism and the immune system, and how it coordinates maintenance of healthy tissue function," said Emily Goldberg, the postdoctoral fellow in comparative medicine who discovered that the keto diet expands gamma-delta T cells in mice.

If the ideal length of the diet for [health benefits](#) in humans is a subject

for later studies, Dixit said, discovering that keto is better in small doses is good news, he said: "Who wants to be on a diet forever?"

More information: Emily L. Goldberg et al. Ketogenesis activates metabolically protective $\gamma\delta$ T cells in visceral adipose tissue, *Nature Metabolism* (2020). [DOI: 10.1038/s42255-019-0160-6](https://doi.org/10.1038/s42255-019-0160-6)

Provided by Yale University

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