Researchers studying diet composition, with no weight loss, to treat Type 2 diabetes

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The study, led by Barbara Gower, Ph.D., is the first randomized clinical trial of a hypothesis that reducing fat stored around organs, through diet alone, can rescue beta-cell function. Credit: University of Alabama at Birmingham

A clinical trial now enrolling at the University of Alabama at Birmingham is taking an unusual approach to help patients with Type 2 diabetes. Instead of medications, the study is using diet alone to improve blood sugar control and remodel the body "by re-partitioning energy away from metabolically harmful lipid stores," said Barbara Gower, Ph.D., professor in the Department of Nutrition Sciences.

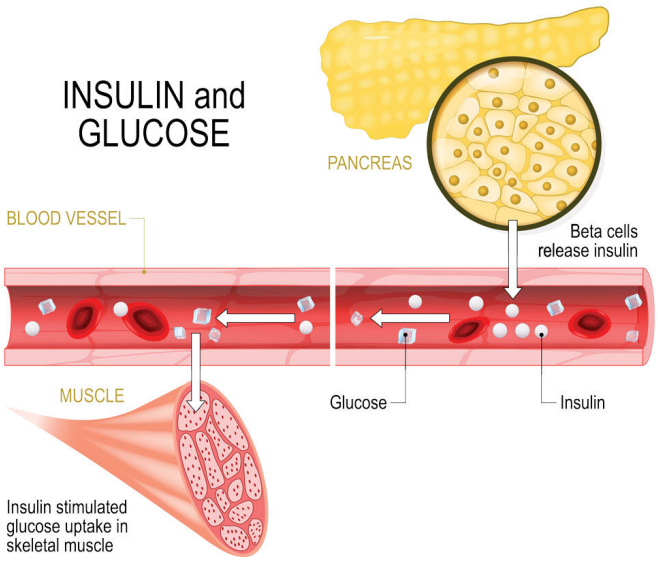
Gower's study, funded by the National Institutes of Health, is the first randomized clinical trial of an intriguing hypothesis. Lipid stored around body organs, particularly the pancreas, damages the beta cells that manufacture and release insulin, Gower believes. In a pilot study, she has already demonstrated that diet modification can remove these lipid stores and dramatically increase the first phase of insulin production in people at high risk for Type 2 diabetes.

For this new study, Gower is recruiting people who have been diagnosed with Type 2 diabetes but are not using insulin. Study participants are assigned to eat one of two diets: a low-fat diet or a low-glycemic diet that is designed to minimize spikes in blood sugar and insulin levels. A low-glycemic diet limits carbohydrates in favor of foods that break down slowly in the body, such as meats, poultry, nuts, eggs, whole grains, and certain fruits and vegetables. All study foods are sent to the participants' homes weekly.

Blind beta cells?

"The main aim of the study is to determine if diet can 'reverse' Type 2 diabetes by restoring beta-cell function," Gower said. Beta-cell function declines progressively in Type 2 diabetes. The decline is especially noticeable in the initial phase of insulin secretion. When you start eating, insulin-packed granules sitting "ready to go" in the outer walls of the beta cells are released within minutes, Gower explained. "If that's not enough, your pancreas can go and get more insulin and package it up; but that takes time," she said. And it is the first phase, the "ready to go" phase, that separates people with Type 2 diabetes from everyone else.

"When you get diabetes, you don't get this immediate release of insulin granules from the beta cells anymore," Gower said. "We inject people with glucose, and nothing happens—after 20 minutes, we start to see a little trickle of insulin; but it takes forever to bring the glucose levels down. Nobody really knows what is happening at the cellular level yet, but what I think is that the beta cells are no longer responding to glucose. It's like they are blind."



Credit: University of Alabama at Birmingham

Effect does not depend on weight loss

This blindness, Gower hypothesizes, might be related to a condition known as lipotoxicity. When we eat more calories than our bodies can use, the excess fat accumulates in and around body organs, including the pancreas. This fat, known as ectopic lipid, is thought to damage beta cells.

There are already ways to reduce ectopic lipid, Gower notes. Both bariatric surgery and very-low-calorie diets have been shown to improve beta-cell function.

In a previous pilot study in Gower's lab, people at risk for Type 2 diabetes who ate the study diet had a nine-fold increase in first-phase insulin secretion, and they had improved blood sugar control as well. Importantly, the diet was designed to maintain each participant's body weight, Gower said: "The effect did not depend on weight loss."

Gower now has funding from the NIH for a much larger study in people with Type 2 diabetes. MRI scans taken during the study will evaluate fat loss around the pancreas. Meanwhile, genetic tests and other samples will help determine "if one diet or the other fits one particular group better," Gower said. "All people with Type 2 diabetes are not the same.

There are patients with beta-cell issues and patients who are more insulin-resistant. We will be able to determine, for example, if the low-fat diet works better for one of those groups and the low-glycemic diet works better for others."

Even greater impact for African Americans?

"Rescue of beta-cell function may be particularly important in African Americans, who as a group demonstrate a high prevalence of Type 2 diabetes for reasons that cannot be explained by lifestyle," Gower wrote in the application for her new trial. "We believe that the disproportionate propensity to Type 2 diabetes displayed by African Americans is due to a unique sensitivity to pancreas lipid."

Published data have shown that pre-diabetes in African Americans is uniquely associated with pancreatic lipid, Gower says. "African Americans display heightened beta-cell responsiveness across the lifespan, rendering them inherently vulnerable to the oxidative stress and endoplasmic reticulum stress that occur with insulin secretion," she wrote in her project description. "We believe that a 'second hit' from lipotoxicity may produce a distinct and particularly virulent disease etiology in African Americans."

If the clinical trial is successful, it could point the way to new recommendations for clinical care of early Type 2 diabetes, Gower says. "An inexpensive, feasible lifestyle change in diet composition may lead to disease remission and/or a slowing of diabetes progression.

Provided by University of Alabama at Birmingham