Health & Medicine

# A Major Victory in the Fight Against Diabetes

Just two weeks of an experimental drug stopped the disease in its tracks.

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Fall 2002

**In a bold new study** led by Columbia's Kevan Herold, M.D., associate professor of clinical medicine, researchers halted the progress of Type 1 diabetes in a group of newly diagnosed patients and kept it in check for over a year—simply by administering two weeks of experimental therapy. When *The New England Journal of Medicine* reported the results last May, a million Americans with the disease and thousands of researchers and physicians around the world did a double take.

Herold is the principal investigator and lead author of the NEJM article. He came to Columbia in 1998 after serving as scientific director for the Juvenile Diabetes Foundation.

His research centers on Type 1 diabetes, formerly known as juvenile diabetes because of its propensity to strike during childhood and adolescence. In Type 1 diabetes, the body's T lymphocytes—the attack dogs of the immune system—somehow lose their ability to distinguish "self" from "non-self" and begin destroying the insulin-secreting cells of the pancreas. Over the years, the relentless autoimmune attack destroys the organ's ability to produce insulin.

Herold's immune therapy was developed by Jeffrey Bluestone of the University of California at San Francisco, who reengineered a monoclonal antibody used in kidney-transplant patients to home in on the relevant T cells in Type 1 diabetes. According to Herold, the new antibodies "alter the signal that otherwise causes T cells to attack insulin-secreting cells." While no one completely understands the nature of this

signal change or how it changes T cell behavior, the net effect is to “bring about ‘tolerance’—teaching the immune system to recognize the insulin-producing cells as self, thereby halting the destructive attack.”

The results of Herold’s study give new hope to a million Type 1 diabetics in this country. Most of them need insulin injections three to four times per day, and all but the most tightly controlled are at high risk for long-term complications of diabetes, such as kidney failure, blindness, and damage to blood vessels and nerves throughout the body.

In Herold’s study, the antibodies were administered to twelve newly diagnosed Type 1 diabetics over a two-week period. A year later, those patients needed less insulin than is typically associated with clinical remission. Moreover, Herold observed an important corollary effect beyond halting the autoimmune destruction: “Patients that received monoclonal antibodies achieved better metabolic control of their disease—and once you achieve better metabolic control, you stop the complications of diabetes.”

Though the therapy in Herold’s study began to lose its effect 18 to 24 months after treatment, Herold is hopeful that the benefits can be extended, perhaps indefinitely, with “booster” treatments. To that end, he has begun a new set of clinical trials. “First, we want to see if multiple treatments with the monoclonal antibodies can prolong the cessation of pancreatic destruction beyond what we achieved in the first set of trials,” he says.

And in a second set of clinical trials just getting under way, Herold plans to use the same monoclonal antibody treatment to try to prevent pancreatic destruction in children and young adults not yet symptomatic but at high risk for developing Type 1 diabetes in the near future. “In patients with antibodies against their own insulin-producing cells whose relatives are diabetic and who have subtle metabolic changes—we know that the majority of those patients will go on to develop Type 1 diabetes,” says Herold. “We’re now going to see if we can keep these young people from ever developing the disease.”

Whether initiated in at-risk patients still able to make sufficient insulin or newly diagnosed patients whose insulin-secreting cells have not yet been fully destroyed, Herold’s immune therapy could revolutionize the treatment of Type 1 diabetes in the not-too-distant future. It even raises new hope for patients whose insulin-producing

cells have been ravaged by years of autoimmune destruction. Immune therapy might be combined with transplantation of insulin-producing cells or stem cells into the pancreases of Type 1 diabetics. If the monoclonal antibodies can keep the destructive process in check, the transplanted cells may be able to assume normal insulin production.

Herold also points out that some researchers believe that insulin-secreting cells may be able to replicate—a phenomenon long assumed impossible. If so, Type 1 diabetes may result when the destruction wrought by the T cells overwhelms the capacity of the pancreas to regenerate sufficient insulin-secreting cells. Collaring the attack dogs of the immune system “may shift the balance toward a net gain in insulin-secreting cells,” explains Herold.

One thing seems clear: Herold’s study has set a new course for researchers. “I’m confident that the picture of diabetes will change in the next five years,” predicts Herold, “and I’m optimistic that with immune therapy, we in diabetes research are finally moving in the right direction.”

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