Could a 100-year-old vaccine treat Type 1 diabetes? MGH researchers are working to find out.

By Jessica Bartlett Globe Staff, Updated March 21, 2022, 7:16 a.m.

Dr. Denise Faustman, director of immunobiology at Massachusetts General Hospital, said BCG appears to help patients with Type 1 diabetes by altering their immune system. ERIN CLARK/GLOBE STAFF

For more than 100 years, it's been jabbed into the arms of children around the world to fend off tuberculosis. Now, a researcher at MGH is testing whether this very old vaccine could help lower blood sugar levels in children with Type 1 diabetes.

The research, led by Dr. Denise Faustman, director of the Massachusetts General Hospital Immunobiology Laboratory, is in its early stages and has proved controversial among diabetes researchers and interest groups. But evidence is growing that the vaccine, called bacillus Calmette Guérin or BCG, can do more than just prevent TB.

Annually, 100 million doses of the vaccine are given to newborns in 84 percent of the world's countries. Because TB isn't common in the United States, children here do not receive the vaccine.

Studies have tied the vaccine to lower rates of childhood mortality and stronger immunity against a host of infectious diseases. There are also signs the vaccine can calm the immune system, benefiting people with allergies and autoimmune diseases.

Around the world, trials are underway to research BCG in multiple sclerosis, Alzheimer's, and COVID-19.

Faustman's lab, in partnership with NYU Langone Health, is recruiting 150 adolescents with Type 1 diabetes for pediatric clinical trials of the shots. All participants must be between the ages of 12 and 17and have to have had the disease for at least two years.

The research builds on studies Faustman has conducted over the last decade.

A small phase 1 clinical trial, published in 2012, showed BCG prompted higher levels of insulin production than in placebo-treated subjects. In a long-term follow of the trial, published in 2018, Faustman's lab found that adult patients with diabetes treated with the vaccine experienced 10 to 18 percent reductions in blood sugar levels and were able to use less insulin. Diabetic patients in the same trial who were treated with a placebo showed almost no improvement.

Research has found that reducing levels of hemoglobin A1c, a measure of blood glucose, by even 10 percent can lower the risk of lifelong complications from diabetes.

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A phase two clinical trial, begun in 2015 with 150 patients, is ongoing, with results expected in a year and a half.

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In individuals with the disease, the body produces abnormal white blood cells that attack insulin-secreting cells in the pancreas.

Faustman's research suggests BCG can turn on "good" white blood cells and destroy "bad" white blood cells prone to attacking the pancreas. Further, the vaccine fixes defects in the white blood cells of diabetes patients, allowing the cells to process sugar and draw more of it out of the blood, Faustman said.

Key to BCG's potency, Faustman and others believe, is the fact that it is a live vaccine. It uses a weakened form of the bacteria that cause tuberculosis, reintroducing a key microbe to the body that humans stopped interacting with as society became more hygienic.

"It's amazing to think about how a bug could, over a period after vaccination, reprogram cells in permanent ways that result in immune responses," Faustman said.

Faustman's research, which is still in early stages, has met with controversy.

After she published her phase 1 research in 2018, JDRF, formerly known as the Juvenile Diabetes Research Foundation, and the American Diabetes Association issued a joint statement saying it wasn't clear that lowered insulin levels were a direct result of the vaccine, as levels tend to change over time, and said the small number of participants wasn't robust enough to be generalized to the larger population.

In a statement to the Globe, JDRF said its position on Faustman's research had not changed.

The ADA did not respond to a request for comment for this story.

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Other researchers also have been skeptical.

“It’s not something being pursued or taken seriously by the rest of the field,” said Stephan Kissler, a Type 1 diabetes researcher at Joslin Diabetes Center.

Other more mainstream diabetes experts are pursuing avenues such as immunosuppression and creating insulin-producing cells out of stem cells that can be transplanted back into patients’ bodies. Kissler works to genetically alter transplanted cells so they don’t require recipients to take immunosuppressants.

“We want to change their disease,” said Kissler.

Yet Faustman sees her work as a stepping stone to do just that. The pediatric clinical trial will focus on children who are at an early enough stage in the disease to still have some pancreas function.

“When we go into older people, they have no pancreas reserve,” Faustman said. “So we’re only testing in them what does BCG do to become a better regulator of glucose metabolism. Now, when we go into kids, it tests the ability of BCG to possibly preserve the pancreas as well as change these sugar defects.

“It’s an exciting population to study. You get to see if you stop the immune response, can the pancreas recover or become more stable as well as getting white blood cells to behave.”

Dr. Joseph Bellanti, a professor emeritus of pediatrics and microbiology-immunology at Georgetown University Medical Center, said the work is innovative and the clinical trials conducted so far were “encouraging.”

“People are entitled to their opinions. My opinion is they are on to something. And it’s worthy of being pursued,” he said.

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Ultimately, Faustman hopes to begin another set of clinical trials by the end of this year in children who have just been diagnosed with diabetes, which could change the course of the disease even earlier.

She is undeterred by the skepticism, saying the number and scope of clinical trials involving BCG speaks to its promise.

“When you see a global momentum to study these off-target effects in humans, you start to see the validity of reintroducing this microbe,” Faustman said.

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