

BCG vaccine leads to long-term blood sugar improvement in type 1 diabetes patients

June 21 2018



Credit: National Cancer Institute

Long-term follow-up of participants in clinical trials of a generic vaccine to reverse advanced type 1 diabetes finds significant clinical benefits, including restoration of near-normal blood sugar levels. Three years after receiving two administrations of the bacillus Calmette-Guérin (BCG) vaccine four weeks apart, all members of a group of adults with longstanding type 1 diabetes showed an improvement in HbA1c to near

normal levels—improvement that persisted for the following five years. The study from a Massachusetts General Hospital (MGH) research team—published in *npj Vaccines* - also reports that the effects of BCG vaccine on blood sugar control appear to depend on a totally novel metabolic mechanism that increases cellular consumption of glucose.

"This is clinical validation of the potential to stably lower blood sugars to near normal levels with a safe vaccine, even in patients with longstanding disease," says Denise Faustman, MD, Ph.D., director of the MGH Immunobiology Laboratory , principal investigator of BCG clinical [trials](#) at MGH and senior author of the *npj Vaccines* report. "In addition to the clinical outcomes, we now have a clear understanding of the mechanisms through which limited BCG vaccine doses can make permanent, beneficial changes to the immune system and lower blood sugars in type 1 diabetes."

Faustman will also present five-year follow-up results of a separate group of BCG clinical trial participants with longstanding type 1 diabetes on Saturday, June 23, at the 78th Scientific Sessions of the American Diabetes Association in Orlando.

Used for almost a century to prevent tuberculosis, BCG has been known for more than 30 years to boost production of a cytokine called tumor necrosis factor (TNF), which may be beneficial in autoimmune diseases both by eliminating the autoreactive T cells that attack an individual's tissues—in the case of type 1 diabetes, pancreatic islets—and by inducing production of regulatory T cells (Tregs) that could prevent an autoimmune reaction. Faustman's team first reported in 2001 that inducing TNF production could cure type 1 diabetes in mice, but since TNF dosing is toxic in humans, clinical trials have utilized BCG for its ability to elevate TNF levels safely.

Initial clinical trial results, published in a 2012 *PLOS One* paper,

reported that two doses of BCG spaced four weeks apart led to reductions in autoreactive T cells, an increase in Tregs and what turned out to be a transient increase in insulin production. But by the end of that short, 20-week trial, there was no reduction in HbA1c, the established measure of [blood sugar levels](#) over time. An extension and expansion of that trial with long term follow-up, the current results are based on data from 282 human study participants—52 with type 1 diabetes who participated in the BCG clinical trials and 230 who contributed blood samples for mechanistic studies.

Regular monitoring of clinical trial participants found that HbA1c levels of those receiving BCG had dropped by more than 10 percent at three years after treatment and by more than 18 percent at four years. That reduction was maintained over the next four years, with treated participants having an average HbA1c of 6.65, close to the 6.5 considered the threshold for diabetes diagnosis, and with no reports of severe hypoglycemia. Participants in the placebo group and in a comparison group of patients receiving no treatment experienced consistent HbA1c elevations over the same eight-year time period.

In investigating how BCG administration produces its beneficial effects, the research team identified a mechanism never previously seen in humans in response to treatment with any drug—a shifting of the process of glucose metabolism from oxidative phosphorylation, the most common pathway by which cells convert glucose into energy, to aerobic glycolysis, a process that involves significantly greater glucose consumption by cells. The researchers also found that BCG could reduce [blood sugar](#) elevations in mice that were caused by means other than autoimmune attack, raising the possibility that BCG vaccines could also be beneficial against type 2 [diabetes](#).

Mihai G. Netea, Ph.D., professor in the Department of Internal Medicine at Radboud University Medical Center in the Netherlands, says

of this study, "The clinical effects and the proposed mechanism demonstrated are exciting and add to the emerging consensus that the BCG vaccine can have a lasting and valuable impact on the immune system. We know, and this study shows, that BCG vaccination induces epigenetic reprogramming at the chromatin architecture level and functional alterations indicative of a permanent change in immunity. The MGH trials and other, larger prevention and intervention trials underway around the globe may lead to a major shift in the prevention and treatment of infections and autoimmunity." Netea was not involved in the current study.

More information: Willem M. Kühtreiber et al, Long-term reduction in hyperglycemia in advanced type 1 diabetes: the value of induced aerobic glycolysis with BCG vaccinations, *npj Vaccines* (2018). [DOI: 10.1038/s41541-018-0062-8](https://doi.org/10.1038/s41541-018-0062-8)

Provided by Massachusetts General Hospital

Citation: BCG vaccine leads to long-term blood sugar improvement in type 1 diabetes patients (2018, June 21) retrieved 20 September 2024 from <https://medicalxpress.com/news/2018-06-bcg-vaccine-long-term-blood-sugar.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--