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Keep That 1876 Journal Handy, It Just May Help Treat Diabetes

By JACOB GOLDSTEIN

A Harvard researcher hopes an old arthritis drug, which he read about in a 19th century German medical journal, could be a cheap new treatment for diabetes.

In the late 1990s, Steven Shoelson's research suggested that the drug, called salsalate, might also help diabetics. The idea sent him into the basement stacks of a Harvard library to see whether anyone else had pursued the notion.

He found an 1876 article published in a German medical journal that suggested salsalate might improve diabetics' ability to control blood sugar. "It was then that I said, 'Aha! We're on to something big,'" Dr. Shoelson recalled.

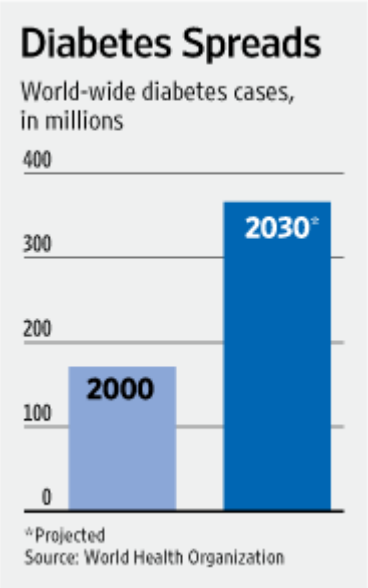
Since that rediscovery, Dr. Shoelson and his colleagues at the Harvard-affiliated Joslin Diabetes Center have seen promising results from several small studies of Type 2 diabetes -- the most common form of the disease. A large study funded by the National Institutes of Health was launched late last year.

If the research bears fruit, the use of an inexpensive and already familiar drug like salsalate could benefit patients not only in the U.S., but also in developing countries where diabetes is on the rise and where costly medicines are unaffordable for many.

Diabetes raises the risk of everything from heart attacks to kidney failure, and the rapid spread of the disease is a key driver of health costs in the U.S. and beyond. But using medicine to control the disease can radically reduce many of the risks.

"It's a cheap, generic drug that has the potential to add to our tools for improving glucose control in diabetics," says Myrlene Staten, an NIH scientist who has overseen some of the agency's funding for the research. "Improving glucose control lowers the cost of diabetes treatment and the risk of complications and hospitalizations."

Salsalate is an anti-inflammatory drug. It blocks a chemical pathway Dr. Shoelson believes may be a key link between inflammation and diabetes. But diabetes experts disagree over whether inflammation is an important factor in the disease.



Stephen O'Rahilly, a diabetes researcher at Cambridge University and self-described "inflammo-skeptic," points out that about a dozen genes have been identified as risk factors for Type 2 diabetes-and none seems to be related to inflammation. For the most part, the genes relate to the ability of the pancreas to produce insulin, a protein that is essential for the body to process sugar. Dr. O'Rahilly, who consults for several pharmaceutical companies, has a friendly bet with Dr. Shoelson -- a bottle of champagne -- over whether the inflammation hypothesis will pan out.

Inflammation traditionally has been seen as the body's response to infection or injury. But as researchers have identified the chemical pathways associated with inflammation, they have found signs of inflammation connected to other factors. Obesity, for example, tends to cause chronic, low-grade inflammation.

That inflammation, Dr. Shoelson believes, makes insulin less effective. Most people are able to produce more insulin to overcome this problem, but those with genetic risk factors for diabetes aren't able to do so, and they develop the disease. Using salsalate to reduce inflammation could break this chain.

In a set of small studies with about 30 diabetic patients, the drug significantly lowered spikes in blood sugar, according to a 2008 article in the journal Clinical and Translational Science by Dr. Shoelson and his colleagues.

Another study was conducted last year and included more than 100 diabetics randomly assigned to receive either salsalate or a placebo. The results haven't been published yet, but they were promising enough to convince the NIH to fund a yearlong trial with more than 400 patients.

That study is likely to provide the clearest picture yet of whether salsalate holds promise in treating diabetics. But it probably won't be enough to provide the clear answers about both safety and effectiveness that would be required to win salsalate's approval from the Food and Drug Administration as a diabetes treatment.

Since salsalate already is sold as an inexpensive, generic arthritis medicine, pharmaceutical companies have little financial incentive to fund research. The Joslin center, which has received at least two patents based on Dr. Shoelson's research, is considering seeking support from foundations for the large, multiyear studies that could be required for FDA approval. Dr. Shoelson says he has no financial stake in salsalate's development.

"We really want to see it remain inexpensive," says Allison Goldfine, who is overseeing much of Joslin's clinical research into salsalate.

Salsalate carries a safety warning, shared by many painkillers, that it may increase the risk of heart attacks

and strokes. But the drug works differently than the other painkillers in the class, and there is no clear evidence that it shares that risk.

In fact, another NIH-funded study Dr. Shoelson's group is working on seeks to determine whether the drug lowers the risk of heart disease by slowing the buildup of plaque in the arteries around the heart.

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