Developing new drugs to treat diabetes

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Drugs based on gut hormones help diabetes patients avoid weight gain. Credit: Wolfgang Krauss, photoexpress.com

The Canadian Diabetes Association reports that nine million Canadians live with diabetes or prediabetes and that 20 new cases are diagnosed every hour.

In this part of the series on research into the exploding global epidemic, we speak to Daniel Drucker, professor in the Department of Medicine at U of T and investigator at Mont Sinai Hospital's Samuel Lunenfeld Research Institute. Drucker studies gastrointestinal hormones and is internationally-renowned for research breakthroughs that have led to a new class of drugs for the treatment of type 2 diabetes.

In past instalments of this series we've looked at the role of diet and exercise in treating type 2 diabetes.

When would a physician typically add drugs to a patient's treatment regime?

There is no one answer. The decision to intervene depends on how old the patient is, what you believe their risk of complications is and how willing they are to follow your recommendations.

Let me give two examples. One is a 90-year-old woman who's been healthy her entire life. She visits her family doctor and is told her blood glucose is mildly elevated. She doesn't have any symptoms of thirst or excess urination, she has no high blood pressure, has never had a heart attack or stroke and is not overweight. She's still active. Do we really need to put her on drugs, even though her blood glucose is slightly higher than all guidelines say it should be? We have no data to suggest that if we put a 90-year-old on medication to try and normalize blood sugar, it's going to help her.

On the other hand, a 35-year-old might come in with a lower blood glucose than our 90-year-old. But he's a little overweight, his blood pressure is up and there is a family history of diabetes, heart attack and stroke. If I can't get him to change his risk factors dramatically, he's going to get into big trouble. Hence, we would probably be more aggressive about starting medications in this individual.

It's important to note that when we treat diabetes we treat the blood glucose, but we also treat associated risk factors. We want people to exercise, stop smoking, and control their blood pressure and cholesterol. We want them to be as healthy as possible. This is tremendously important for preventing complications, rather than just focusing on blood glucose. Nobody gets up in the morning and says, "my blood sugar is 10 millimolar and it really hurts." But we know that, over time, that person is going to have increased risk of kidney disease, blindness, blood

vessel disease, heart attacks and strokes.

What is the difference between treating type 2 diabetes with medication versus insulin?

A lot us feel that insulin might be the best drug to treat type 2 diabetes. There's a study that's going to be reported soon that will examine the results of people who were treated from the start with aggressive insulin. My colleague Dr. Bernard Zinman has investigated this topic. And in many parts of the world people do initiate insulin as the first therapy for type 2 diabetes because they believe it's the best.

But in North America we commonly start with oral medication before insulin. The reality is that many people don't want to go on a daily injection, even though the needle is small and painless. Most people would rather take a pill.

Does medication or insulin therapy stop diabetes?

No. Diabetes is a progressive disease. There has not yet been a therapy or intervention that can prevent the disease from progressing. Diet and exercise can slow it down. Some medications can slow it down. Early insulin use may slow it down. But we have no therapy that will stop the disease in its tracks.

Your work has led to the development of a new type of drug. Tell us about it.

I've spent my career working on gut hormones. These are the hormones our gastrointestinal tract makes, predominantly in response to food ingestion. They help us sense when we're eating, absorb nutrients like glucose and then dispose of them. They also regulate appetite by sending

signals to the brain.

Since these hormones are so important in terms of how much we eat and what happens to the nutrients we ingest, it wasn't a big leap to think maybe we could exploit their actions when we have a problem with eating too much, with high blood sugar or with nutrients that are not being absorbed, which is essentially what happens with obesity and type 2 diabetes.

We and others discovered the first actions of these hormones 25 years ago. I was a postdoctoral fellow in Boston then. Now there are two classes of medications based on them. One of these drugs, a DPP-4 inhibitor, may be the world's bestselling diabetes drug next year.

How do drugs based on gut hormones differ from conventional drugs? Will they actually be able to stop the progression of type 2 diabetes?

There is ongoing research to determine whether they will be more durable and on whether they will reduce heart attacks or strokes. So we don't know yet.

But what we can promise now is that patients will have fewer hypoglycemic events and they will not gain weight as a side effect, in contrast to most of the other drugs. The way we treat type 2 diabetes is a little disingenuous. We bring a person in and put them on the scale. The average type 2 diabetes patient is overweight or obese. So we tell them to lose weight. Then we write them a prescription for a diabetes drug that causes weight gain. They're back three or four months later, and we tell them we're disappointed they haven't lost weight. That won't happen with these drugs. In fact, there's a lot of evidence that they promote weight loss.

The other big advantage is that these drugs are easier for patients. They don't need to adjust the dosage frequently. They don't need to check their glucose levels by pricking their fingers four times a day.

You're being celebrated this year by the European Association for the Study of Diabetes for discovering these gut hormones 25 years ago. Did you foresee the impact that discovery would have?

No. It's important to understand how long it takes for basic science to be translated. We published the first paper about the hormone GLP-1 in 1987. After that, it took lots of folks years and years to figure out how it all worked. The first GLP-1 drug was approved in the United States in 2005.

That's how long it takes. You can never predict the outcome of basic science. All you can do is create a culture of innovation. You have to put in place the funding, the tools and the opportunities and then you have to let good people do what they're good at. And then good things will happen. If you support basic science, whether it's medicine, biology, physics, chemistry or agriculture, you're going to have a payoff, but it's not going to be evident within the next electoral cycle. It's not a short term thing. But if you have vision and put in place a strong foundation, it will pay off.

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