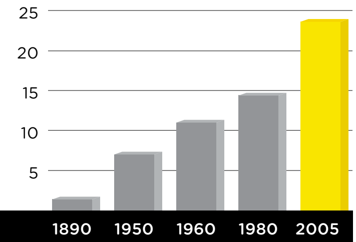
Incidence of type 1 diabetes per 100,000 children.

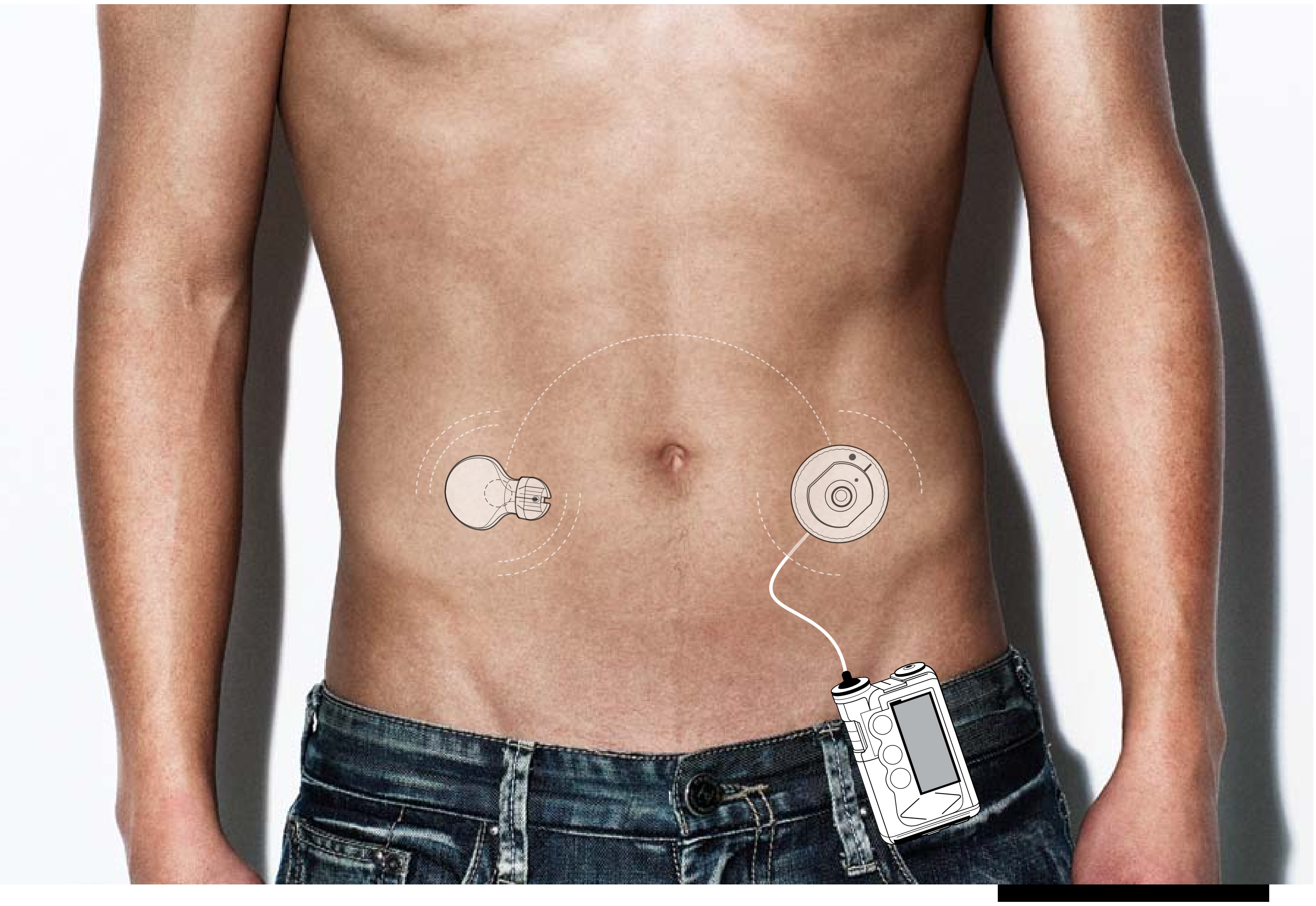


The Robotic Pancreas

One man's quest to put millions of diabetics on autopilot.

BY DAN HURLEY

18.05



Artificial pancreas: An implant feeds blood-sugar data to a pump that automatically administers insulin.

JEFFREY BREWER WAS on top of the world. For years he had put in 100-hour workweeks as cofounder of two early Internet juggernauts: local guide Citysearch and the online advertising pioneer GoTo.com (later renamed Overture). But by 2001, with more than enough money to live on for the rest of his life, the 32-year-old handed off control of Overture and set out on a yearlong trip to Australia with his wife and two kids. Upon their return to the States, though, they noticed something odd. Seven-year-old Sean was unquenchably thirsty and urinating far more often than usual. On September 19, 2002, they took him to the pediatrician. The doctor gave him a urine test and announced without hesitation, "Your son has type 1 diabetes." ¶ Previously known as juvenile diabetes because it is usually diagnosed before adulthood, type 1 is the "other" kind of diabetes, the kind no amount of dietary adjustment will hold at bay. It develops rapidly, due to a mysterious autoimmune

ILLUSTRATION BY JAMESON SIMPSON; GROOMING BY VERONICA SJOEN/ARTIST UNTIED

PHOTOGRAPH BY Stan Musilek

reaction that attacks the insulin-producing beta cells in the pancreas. Treatment requires insulin injections and relentless hour-by-hour diet control. Short-term, the main risk is hypoglycemia—low blood-sugar level caused by too much insulin—which makes patients exhausted and confused, leading to unconsciousness and death if not treated immediately with something sweet. But the opposite problem, high blood sugar, raises the long-term risks of kidney failure, blindness, amputation, and heart disease. Either way, type 1 diabetics live on the edge, a cupcake away from a coma.

Nurses taught the Brewers how to inject the insulin and how to prick Sean's finger for the drop of blood to test his blood-sugar level with a little meter. They learned a simple algorithm: If their son's blood sugar was this high, give him so many units of insulin; if it was this much higher, give him that much more. It's a crude scale that every one of the more than 1 million type 1 diabetics in the US makes do with daily.

Tall, thin, and intense, Brewer was shocked by the antiquated approach. "I had this logbook," he says. "I'm testing Sean every few hours, and I'm thinking, this is crying out for automation. A computer should do this and would do it better. Why didn't this exist, with all that we can do?"

So began phase II of Brewer's life. He would become advocate-in-chief for bringing to market a breakthrough technology that has been promised for decades: a fully automated, self-regulating artificial organ—mechanical and electronic rather than biological—that would sense blood-sugar levels continuously and release just the right amount of insulin at just the right time without the need for any action, or even awareness, on the patient's part. Good-bye to many-times-daily blood tests. Farewell to insulin injections containing back-of-the-napkin dosages and inevitable hours of feeling ill. Good riddance to the risk of slipping into unconsciousness and an untimely death. Brewer would start the race to build a technological fix for diabetes. The biggest obstacle? Bureaucratic logjams.

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EVERYONE, BREWER soon found out, had an excellent reason for not letting Sean and other diabetics fly on autopilot. Manufacturers were afraid of liability, academics were bent on achieving perfection, and the Food and Drug Administration was downright jumpy at the thought of letting a computer control a mechanism with life-and-death responsibilities.

Yet most of the components for what researchers were calling an artificial pancreas—an external device the size of an iPod that would duplicate the insulin-secreting and -regulating functions of that organ—were already in place. An insulin pump had been approved back in the late 1970s, and a continuous glucose monitor that read the output of a sensor implanted under the skin was nearing approval. (The first one would hit the market in 2005.) The trick was to connect the two via software, letting the monitor's information on blood-sugar levels—high or low, rising or falling—serve as the basis for calculating exactly how much insulin to release.

Brewer flung himself into the challenge with the same passion he had brought to his Internet startups. Less than a month after his son's diagnosis, at a meeting of the Diabetes Technology Society, he was ready to shake things up. After listening to an arcane academic debate about which algorithm would be best for the pump, Brewer stood up in the audience and began berating the scientists for dithering over details. "We have all the pieces," he said. "We need to start commercializing these technologies, because people living with the disease need it."

The audience broke into applause.

Then Brewer hit the road, traveling to the leading manufacturers in diabetes technology. He joined the board of the Juvenile Diabetes Research Foundation.

"I remember it vividly," says Aaron Kowalski, the JDRF's assistant vice president for glucose control research, about the first time he witnessed one of Brewer's applause-inducing interruptions. "It was amazing. I've been to many, many scientific meetings, and I don't know that I've ever seen anything like that happen before."

Kowalski is a big, friendly guy who is himself a type 1 diabetic. He quickly found in Brewer a simpatico spirit who shared his vision for a smart insulin pump. The JDRF, however, had devoted itself since its founding in 1970 to discovering a biological cure, not a technical solution. But Brewer would not be dissuaded. Late in 2004, at a JDRF board meeting, he issued a challenge: He would donate $1 million to the organization if it would commit to getting such a device commercialized.

In early 2005, the board told him that the JDRF might be willing if he could assure them the smart pump wasn't just a pipe dream. In October, after months of investigation, Kowalski and Brewer presented their plan to the board, which voted to approve the foundation's new Artificial Pancreas Project.

SPURRED BY THE INFLUX of money and attention, progress came quickly. In 2008, researchers at Yale reported results from one of the first human trials of a computer-controlled glucose monitor and insulin pump. When their subject group of 17 teens managed their own pumps, the Yale team found, their blood-sugar levels were above 180 (moderately high) one-third of the time and below 70 (the point where many people begin feeling woozy and disoriented) 9 percent of the time. By comparison, when the computer did the driving, the same teens were above 180 only 15 percent of the time and below 70 only 3 percent of the time, putting them in the target zone a whopping 82 percent of the time.

But just one study of 17 teens in a laboratory setting is not enough. Much more work was needed before the FDA would even consider approving such a device.

Less than a month before the Yale study was published, Boris Kovatchev, head of computational neuroscience at the University of Virginia, Charlottesville, persuaded the FDA to let him bypass animal studies for each new version of the device and instead rely on "in silico" studies—computer simulations.

"Simulation can actually be more useful than an animal study," he says. Perhaps better than anyone else, Kovatchev knows that getting a computer to regulate blood-sugar levels is a daunting task: "It's infinitely complex, because the blood-sugar level is constantly changing."

Adding to the difficulty is the lag between a diabetic's current blood-sugar level and the readings transmitted by the glucose monitor, not to mention its margin of error. Moreover, once the insulin is released, it takes at least 15 minutes to begin lowering sugar levels, reaches peak efficiency after 45 minutes, then continues working less and less efficiently for another three hours. So the job of the automated insulin-dispensing system can be likened to navigating a car down a winding road when you're unable to see the curves until you're 15 yards past them—and turning the steering wheel has no effect for another 200 yards.

By April 2009, Kovatchev was running the largest clinical trial yet, in collaboration with researchers in France and Italy. (Disclosure: As a type 1 diabetic, I was a volunteer in Kovatchev's study.) Among the 10 diabetics he personally tested during overnight stays, he says, there were 17 episodes of mild hypoglycemia when the patients controlled their own insulin pumps, compared with just two when the device was in control. That's an eightfold reduction—for most typical situations, computers really are better than humans at dispensing insulin in response to shifting blood-sugar levels.

NOW THE MAIN CHALLENGE is getting the FDA to recognize that fact. In June 2009, Medtronic, a leading maker of diabetes treatment devices, announced the approval in several European countries of an integrated pump and sensor with a "low glucose suspend" feature that shuts off the pump when sugar levels are dangerously low. While only a baby step toward a fully self-regulating unit, it represents a milestone. But the FDA was still demanding that Medtronic conduct a clinical trial of the automatic shutoff before the agency would approve the device.

The delay has left Brewer fuming. The FDA, he says, "has a skewed way of looking at these kinds of products. They are worried about the theoretical safety issues, but that ignores the greater danger from existing pumps."

Indeed, because current pumps are designed to deliver a small amount of insulin around the clock, they will do so even if a diabetic is unconscious with severe hypoglycemia—still digging the hole, as it were, until it becomes a grave. To guard against that very real possibility, parents like Brewer routinely wake during the night to check their child's sugar level.

A recent JDRF-financed study at the University of Cambridge showed the benefits of an artificial pancreas in that very situation: Researchers found that during overnight monitoring, a computer-controlled system kept type 1 diabetics in the blood-glucose target area as much as 78 percent of the time, compared with just 48 percent when using a manual insulin pump. The study bolstered enthusiasm for the device.

At this point, Brewer has devoted nearly as much time to the artificial pancreas as he did to Overture. He confesses that speeding the FDA's decisionmaking process might eventually require the kind of marches and protests that other advocacy groups have used.

For its part, the FDA insists it is moving as fast as possible and that its caution is justified. "The approval process in Europe is not anywhere near as rigorous as it is in the US," says Arleen Pinkos, who leads the agency's Artificial Pancreas Critical Path Initiative. "We've had what might be seen as a slow start, but with new product lines, it's normal for the FDA to start slowly and move faster as we gain experience. We have made tremendous advances behind the scenes, and a lot of that has to do with the JDRF," which spent approximately $10 million on research last year and has lined up another $15 million for 2010.

People suffering from type 1 might not wait for the agency to act. Some have begun whispering about hacking their pumps to control them wirelessly. The likelihood of someone actually doing that increases with each passing day of bureaucratic paralysis.

This much, then, is clear: The artificial pancreas is no longer the jet pack of diabetes, talked about for decades without ever coming to fruition. For all their frustration, Brewer and Kowalski are confident the FDA will approve a semi-automated insulin dispenser within five years.

Then, perhaps, it will be time for Brewer and his family to take another year off.

Adapted from Diabetes Rising: How a Rare Disease Became a Modern Pandemic, and What to Do About It, *copyright ©2010 Dan Hurley.* **DAN HURLEY** (hurleydan@aol.com) *is a medical journalist and a type 1 diabetic.*