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Dr. Denise Faustman had reported the pancreas might cure itself.

A Controversial Therapy for Diabetes Is Verified

By GINA KOLATA

Three groups of scientists report today that they independently replicated a controversial finding: severely diabetic mice can recover on their own if researchers squelch an immune system attack that is causing the disease.

It is a discovery that was first published in 2001 and raised the hopes of people with Type 1 diabetes, which usually occurs in puberty and afflicts an estimated half-million to a million Americans. If the findings applied to humans, they might mean reversing a disease that had seemed incurable.

The findings also gave rise to questions about using embryonic stem cells as replacement cells for diabetics, a method that is the focus of intense interest. If it is possible, in mice, for the pancreas to cure itself, and if the same finding holds true in humans — which, so far, is entirely unknown — adding embryonic stem cells as the source of new pancreas cells might provide little added benefit, if any.

In any event, scientists are not yet ready to treat diabetic patients with embryonic stem cells; they first have to prod the cells to turn into insulin-secreting pancreas cells. Meanwhile, efforts to cure diabetes by transplanting pancreas cells from cadavers have met with limited success.

The report several years ago, by Dr. Denise Faustman of Massachusetts General Hospital, that the pancreas might cure itself, at least in mice, met with skepticism.

"People just didn't believe it," said Dr. David Nathan, director of the diabetes center at Massachusetts General and a longtime supporter of Dr. Faustman. "People said you can't cure diabetes."

But, Dr. Nathan added, "this shows that at least in mice it has been confirmed and reconfirmed and confirmed again."

The three new papers, by researchers at the University of Chicago, Washington University in St. Louis, and Harvard's Joslin Clinic are published today in Science. In every case, the investigators followed Dr. Faustman's procedures, injecting diabetic mice with Freund's Complete Adjuvant, a mixture of water, oil and parts of dead bacteria. It overstimulates the immune system cells that are attacking the pancreas, making those white blood cells self-destruct, effectively stopping the attack and allowing the pancreas to cure itself.

The different groups calculated their cure rates in different ways but all reported that a significant proportion, though less than half of the mice, were cured. In Dr. Faustman's experiments, 67 percent of the mice were cured.

Dr. John Buse, director of the Diabetes Care Center at the University of North Carolina, urged caution.

"There are two possibilities," Dr. Buse said. "This treatment works for mice but no derivation of it will ever work for humans. Or this is the paradigm leap that is necessary to find the cure for Type 1 diabetes."

"If I was a betting person, my guess is that it probably won't work in humans," Dr. Buse added, explaining that all too often in science what works in mice does not work in people.

And despite their success in curing some of the mice, the three groups of researchers could not confirm another of Dr. Faustman's findings, published in Science in 2003. There, she reported that the new insulin-secreting cells came from the spleen. Dr. Faustman added that she could boost the animal's response to her treatment by giving them extra spleen cells, although, she said, the extra cells were not necessary to cure the mice. Just stopping the immune system attack was sufficient, she said.

Most scientists questioned the spleen cell finding just as they questioned Dr. Faustman's claims that she could cure mice with advanced diabetes in the first place.

In the meantime, Dr. Faustman attracted the attention of Lee Iococca, who recently raised $11 million for her medical center for studies testing her initial discovery in humans. Patients clamored to be included. Even though she is not ready to begin even the most preliminary tests, she already has 600 on a waiting list.

Diabetes researchers have long known that the Type 1 form of the disease is caused when the immune system attacks insulin-secreting beta cells that reside in islets, round balls of cells, in the pancreas. And they realize that they have to stop that attack if they are ever to cure the disease. But, said Dr. Jeffrey Bluestone, director of the Diabetes Center and Immune Tolerance Network at the University of California, San Francisco, most investigators have assumed that curing diabetes, even in mice, requires providing new pancreas cells after the immune system is tamped down.

"What these papers suggest is that there may be some capacity inside the animals to make new beta cells without doing a transplant," Dr. Bluestone said.

"It says that even a long time after the mice are diabetic, they still have a capacity to develop new beta cells," he added. "That's very exciting."

But the question remains, Where did the new islet cells come from?

The groups from the Joslin Clinic and Washington University say the cells derived from a few beta cells that had survived the immune system onslaught. The Chicago group says its studies could not answer the question.

In a sense, Dr. Bluestone says, it sounds academic. After all, the point is that the pancreas cells came back on their own. The origin of those cells may not matter to patients. But, he said, "we need to be cautious since it may not be straightforward moving these mouse studies into humans."

Dr. Louis H. Philipson, the senior author of the University of Chicago group, concurred.

"If it's the spleen, you have hundreds of thousands of first-degree relatives and parents of diabetics who will be prepared to donate their spleens," Dr. Philipson said. "You have to be very careful what you tell desperate people."

As for Dr. Nathan, he agreed that the spleen question needed to be resolved. But, for now, he added, the real importance was that Dr. Faustman was correct that even severely diabetic mice could be cured.

"The bottom line is that the approach worked," Dr. Nathan said.