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## Diabetes Drug Shows Promise in Insulin-Cell Transplants

By LAWRENCE K. ALTMAN

Scientists reported yesterday that they had cured diabetes in monkeys by giving them transplants of insulin-producing cells along with an experimental drug that prevented rejection of the donor tissue.

The findings are an important advance in diabetes research, "strikingly different" from all other previously tested strategies, and a step toward the ultimate goal of curing diabetes in humans, the scientists said. Their findings involving the experimental drug, known as anti-CD154 are to be reported later this year in the Proceedings of the National Academy of Sciences, which made the paper available ahead of publication.

Anti-CD154 is an artificially made antibody intended to thwart a key part of the immune system to ward off foreign tissue.

Experimental trials of the therapy in humans have been approved by ethics committees and the Food and Drug Administration. They are expected to begin soon with support from the National Institutes of Health, said the researchers and the drug's manufacturer, Biogen Inc. of Cambridge, Mass. But they refused to give details like the starting date of the trial or the number of patients to be included.

Dr. Norma S. Kenyon, the lead author of the report from the University of Miami and the Navy, said the

findings represented the most promising advance she had seen in 20 years.

"This may be something that is part of an eventual cure, but we do not want to mislead people by saying we have a final answer at this point and I do not want to raise false hopes," Dr. Kenyon said in an interview.

Nevertheless, Dr. Camillo Ricordi, a co-author of the report, said, "It is a major reason for cautious optimism."

The islet cells, which were transplanted into the monkeys, are the parts of the pancreas gland that produce insulin to control blood sugar. Islet-cell transplants have been carried out in more than 300 people in recent years but with limited success, Dr. Ricordi said. After a year, the graft has functioned in fewer than 35 percent of such patients and fewer than 10 percent have been able to stop taking insulin. Thousands more people have received transplants of the entire pancreas gland, located deep in the abdomen.

However, a major problem with both islet cell and pancreas transplants is that each recipient would have to take a combination of powerful anti-rejection drugs for the rest of his life. The drugs increase the risk of infection and other complications, and can also promote development of diabetes, even in those without the disease.

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**Scientists say tests with monkeys show that a treatment prevented rejection.**

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To the Miami team, the most exciting finding was that they could safely prevent rejection with only one drug, not a cocktail of drugs. Also, the animals grew normally and suffered no infections or other complications. Anti-CD154 did not produce diabetes in the monkeys.

The experiments involved seven monkeys that were made diabetic by removing their pancreas glands.

Seven monkeys received islet cells from other monkeys even though they were severely mismatched in blood and immune tests. The cells were injected through a tube into blood vessels leading to the liver where the cells took up residence. The procedure took about a half hour and could be done as an out-patient procedure in humans, Dr. Ricordi said.

Six monkeys received injections of anti-CD154 on the day before the islet cell transplant, that day and four additional times in the next 28 days. Then the monkeys received anti-CD154 each month thereafter. Islet-

cell function improved over time.

The experiment is intended in part to test whether the islet cells will continue to thrive after anti-CD154 is stopped, a year after the transplant. Three of the six monkeys that have lived for such a period no longer require injections of insulin or anti-CD154. Anti-CD154 will also be stopped when the remaining three reach the one-year anniversary.

Unanswered is the length of time that the recipients of the anti-CD154 islet cell therapy can stay off insulin, the researchers said.

The seventh monkey served as a scientific control and did not receive anti-CD154. That animal began rejecting the islet cells six days after the transplant and needed daily insulin treatment.

In another paper published last week in the journal *Diabetes*, Dr. Kenyon's team reported that anti-CD154 could reverse individual episodes of islet cell rejection in animals if and when they occurred.

Dr. Ricordi said islet-cell transplants had survived for more than eight years in a human liver.

A spokesman for the American Diabetes Association did not return a phone call.

Anti-CD154 has been tested for safety in a small group of people, a spokeswoman for Biogen said. It has also shown promise among monkeys that have received kidney trans-