# Science

# Diabetes Researchers Are Aiming for a Cure

by Miriam Tucker

*The following is part two of a story on current research in insulin-dependent diabetes mellitus.*

Insulin-dependent diabetes mellitus (IDDM) occurs when the beta cells of the pancreas stop producing insulin, a hormone required for carbohydrate metabolism. Victims, who are primarily children, must then take daily injections of insulin to stay alive. Recent developments in diabetes research were presented at the International Symposium on Juvenile Diabetes, held in Tokyo last year. Dr. Allan Drash, a leading expert in the field of childhood diabetes, was one of the participants. He categorizes the many fields of research into the "five C's": cause, course, care, complications, and cure.

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**Diabetic neuropathy can lead to foot problems.**

### Complications

Many long-term complications occur as a result of IDDM, such as kidney damage, atherosclerosis, eye damage, and neuropathy. These complications tend to appear gradually, over a period of many years. For instance, there is evidence that increased frequency of early eye changes exists in patients who have shown higher levels of glycosylated hemoglobin. The degree of glycosylation is directly related to the amount of excess sugar in the blood over a period of time. The evidence suggests, therefore, that there is a relationship between control of sugar levels, and the incidence of diabetic retinopathy. This disease causes a gradual clouding of the retina, which can lead to blindness if left untreated. There are, however, many patients who have poorly controlled blood sugar levels, yet show no evidence of any eye changes. This implies that there are environmental or genetic factors which could either enhance or protect against retinopathy.

Other long-term complications, such as neuropathy, microangiopathy, and cataracts are thought to be due to the process of glycosylation of several different proteins in the body. This process, which occurs in elevated levels in diabetics, is thought to destroy tissues over time.

### Cure

The search for a cure for diabetes mellitus is the major focus of many research centers around the world. As yet, however, there is no such thing as a cure for IDDM. The three main areas of interest are: transplantation of whole pancreases or of isolated beta cells, immunosuppression at the time of diagnosis, and wearable or implantable insulin pumps.

Eight human pancreas transplant operations have been performed in Pittsburgh by Dr. Thomas Starzl. Six of these have proved successful; these patients can be considered cured of diabetes. Work in beta cell transplants is being done in St. Louis and Miami, where doctors have used this method successfully to cure diabetic dogs. Beta cell transplant attempts in humans, however, have not been successful.

The major problem of transplantation is one of number. In this country there are five million diabetics, at least ten percent of whom are insulin-dependent. In addition to these potential recipients, 20,000 new cases of IDDM are diagnosed every year. The only source of transplantable pancreases are from people who have suffered brain death, in which the tissues of the body were functioning long enough to be removed and prepared for transplant.

Out of 20,000 brain deaths that occurred last year, only ten percent yielded transplantable kidneys. The number of pancreases obtained would be even less, since they tend to die much more quickly than hearts or kidneys due to the digestive enzymes they contain. Therefore, approximately 1,000 to 2,000 diabetics can be cured per year by whole pancreas transplants. This is a drop in the bucket compared to the 500,000 or more IDDM patients in the U.S.

It would seem that the beta-cell transplants would ease the situation, since only the insulin-producing cells of the pancreas are being used. However, the number problem here is actually worse. With the extraction techniques we have today, two or three pancreases are usually needed to obtain enough cells for one transplant. Ideally, if beta cells could somehow be induced to replicate, the problem would be solved. However, cells which replicate in a test tube could conceivably replicate in the body, which would be a type of cancer. Therefore, Drash is not very hopeful about the future of transplants as a widespread cure for IDDM.

The only patients who are currently considered for pancreas transplants are those who already need immunosuppressive therapy for some other aspect of their diabetes, such as for kidney transplants. For the majority of otherwise healthy diabetics, however, Drash is looking elsewhere for cures.

Another major area of development is the insulin pump, of which there are two distinct types. One, developed in the late 70's, is the open-loop pump, worn outside the body and attached by a needle inserted into the abdomen. This pump delivers a constant basal amount of insulin, but the patient must also "pulse" it with an additional amount of short-acting insulin before each meal. The patient, therefore, must still test his blood for glucose to determine how much to "pulse" himself. This method is highly erratic and subject to a large amount of error.

A newer development, the implantable pump, looks much more promising. Two types are

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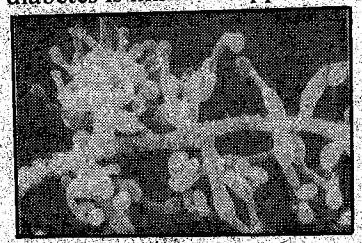
currently being tested. One, developed in Japan, is implanted into the abdominal cavity along with a glucose sensor, which detects the level of glucose in the blood. A tiny computer contained in the unit then determines the amount of insulin to be released. This model is due for commercial distribution by the end of 1985. So far, this is the most promising of potential "cures."

Another type of implantable pump is still in the experimental stage in Europe. Called a continuous infusion pump, this model delivers a fixed amount of insulin to the peritoneal cavity. It is thought that since the insulin is delivered more or less directly to the liver, the liver will act as a "thermostat," once it receives a sufficient amount of insulin. It will then release glucose during exercise, or retain it in response to eating. Not much is known about the mechanisms involved in this process; therefore, the continuous infusion pump is still considered experimental.

Another exciting direction in the search for a cure for diabetes is immunosuppressive therapy. A study in Ontario is attempting to determine the effects of using the drug cyclosporin A, which suppresses the body's immune system, on newly diagnosed diabetic children. At the time of diagnosis of diabetes, most victims will still have some beta cell activity, and may go into a temporary remission. The cells die quickly thereafter, though. Evidence suggests that administering cyclosporin during this critical stage may prevent further cell death, thus preventing the patient from becoming diabetic. However, as in the transplant issue, ethical questions arise. Cyclosporin has pervasive effects over the entire body, and it is not known what the long-term effects of the drug are; they may be worse than the effects of diabetes itself. Therefore, researchers are approaching the issue of immunosuppressive therapy with caution.



**Cyclosporin A—a potent new immunosuppressive drug.** JDF

Drash and his staff at the Children's Hospital of Pittsburgh are currently working on aspects of all five major areas of diabetes research, and are making significant headway in perfecting pump therapy and in discovering the etiology of the disorder.

*A support group has recently begun in the Baltimore area for diabetics between the ages of 18 and 24. If interested, please call 467-4079 or 455-2621 for more information.*