Treating Diabetes with Transplanted Cells

Seventy-five years ago the type of diabetes that affected children and young adults was lethal. In the 1990¹s investigators found that a hormone, that was produced in Islets of Langerhans, was not being produced in diabetes patients. This hormone, called insulin, enables other cells to take up sugar glucose from the blood for energy. Diabetes patients who were not making insulin had glucose from food accumulating in the blood while other tissues were starving. Their are two types of diabetes. Type 1 diabetes has ceased completely from making insulin and the people who had this kind usually died. Type 2 diabetes still makes a little insulin so suffers of this type usually lived.

In the 1920¹s prospects for people who suffered from type 1 diabetes increased when it was learned that insulin extracted from animals and placed in humans could prevent death. Unfortunately, this is not a cure. Patients can get potentially fatal diabetes-related disorders. These include blindness and, or kidney failure. Atherososclerosis, numbness and pain in extremities caused by narrowed vessicles, may also be a problem. These effects are caused because insulin injections can¹t perfectly mimic naturally made insulin.

That¹s why a therapy that maintains glucose values within normal from the begging is needed. An ideal treatment would be the implantation of islets. This, in theory, would only have to be done once and would insure proper insulin production. Successful grafts would also prevent diabete-related ills.

At Paul E. Lacy¹s lab, experiments have been done for twenty- five years on such a process. At first they were just trying to understand the mechanics of hormone secretion. To start this they needed a way to separate islet clusters from the pancreas. These constitute only 2% of the entire pancreas, though, and are scattered throughout it. In 1967 they found a solution and took the islets from rats. These islets were transplanted in inbred rats to see if it would control insulin production in diabetes patients. It was a success and kept blood sugar levels normal. It even fixed early complications in the eyes and the kidneys.

The next step was to test the process on humans. Unfortunately, the process that was used to separate rat islets from the pancreas did not work on humans. They had to find a new way to solve the problem. The problem took a few years to solve but in the mid 1980¹s they finally found a semi-automatic method to do it. This method managed to isolate 400,000 islets from the pancreas. It would take just the amount they estimated to maintain the blood sugar level.

In 1986 the first experiment started. A lot of immune-suppresent drugs are needed so the foreign tissue would not be rejected. These drugs are risky, though, so the experiment was performed on patients who have had kidney transplants and are already on these drugs. They decided that the best place to place the islets was into the portal vein leading to the pancreas. This would give the islets nourishment from the beginning and would be less risky than placing them directly into the pancreas.

The results were encouraging. Subjects were given 400,000 islets and the grafts worked. But it was not enough to stop insulin injection. Later when the islets were increased to 800,000, the insulin injections were able to be stopped, at least for a time. They also learned that the islets could be frozen and stored. Since 1990 about 145 patients have had the process done. Most were unable to control the blood sugar level. Strain on the islets may have been a problem and in some cases enough probably weren¹t used.

Doctors are proposing to give these transplants with graphs even though the results weren¹t perfect. The process is less costly and easier than complete pancreas transplantation.

Many concepts have been considered though to solve the last part of the problem. One is being looked into by Kevin J. Lafferty. That is, that if you destroy passenger luekocytes, the tissue would not be rejected.This has been attributed to the theory that it takes two signals for host white blood cells to

attack foreign agents. These two signals are sent by the passenger luekocytes. Unfortunately, to destroy these luekocytes you also destroy the hormone-producing cells. Joseph M. Davie has devised a culturing technique, though, that kills the passenger luekocytes without hurting the hormone-producing cells. He placed 1,500 treated islets from one rat strain to a portal vein of another. There was no rejection! Unfortunately, the individual islets had to be treated separately and so is not practical for humans who need much, much more islets. A solution was found in 1993. It is to take a few treated islets to a subject. This creates a tolerance for these islets which are transplanted untreated later. This is still being experimented on, though.

Another process is being experimented on also. This is being tried because of the theory that diabetes is caused by an autoimmune process that differs from rejection. This process perceives beta cells, specific cells that produce insulin, as foreign tissue and destroy them. Therefore even if a transplant is fully successful the bets cells will be destroyed. To cure diabetes, islets that do not match those of the recipients islets must be injected. Another solution is also to enclose these islets in a semipermeable plastic membrane. If pore size is ideal, membranes let glucose reach islets and allow insulin to made while keeping the islet safe.

William L. Chick developed a technique that puts islets in a plastic tube that allows blood flow in where it contacts the islets. Then insulin passes out. It worked for a while until the tube became clogged. The biocompatibility has been improved, though, and has worked for several months in a dog specimen. These tubes are thought to be able to rupture though in a rough situation. This could cause internal bleeding. The tubes could also clog arteries.

Franklin Lim and Anthony M. Sun has also prepared islets by suspending them in alginate and enclosing them. It has been placed in rats and worked but the islets died from lack of nutrients caused by the alginate. Plastic-coated droplets are more biocampatible and have temporarily reversed diabetes in patients. These capsules are very small but are needed in such large amounts that to be feasibly worked they would have to be even smaller. A way to remove these capsules readily is also needed.

Paul E. Lacy has also developed a way using islets covered in jelled alginate and then enclosed in a hollow, semi spherical acrylic fiber that has amazingly biocompatibility. This procedure maintained normal blood sugar level in a rat for an entire year. It is being tested on humans.

Research is also going on to make a fully artificial pancreas. This device would be able to monitor blood sugar and release just the right amount of insulin in response. A device that is at once small, durable and accurate is still trying to be devised though.

Before these a solution can be wide spread used though, enough donor islets must be found beside cadavers due to the amount of people that suffer from diabetes. Some other places islets might be found are in fetuses, many scientists hope to find a way to implant insulin-making cells alone which can be grown in labs, and pig islets are also a major possibility. Transplanting of encapsuled cells may also help a lot of other people beside diabetes patients including; Hemophiliacs and people suffering from Parkinsons disease.