

# Strategies In Surgery

## A Cure for Diabetes

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Following the discovery of insulin in 1921 by Frederick Banting and Charles Best, diabetes was thought to be a disease of the past. It did not take long, however, to realize that a once rapidly lethal illness was now transformed to a chronic medical condition characterized by major metabolic derangements including renal failure, retinopathy, peripheral neuropathy, coronary artery disease and frequent amputations.

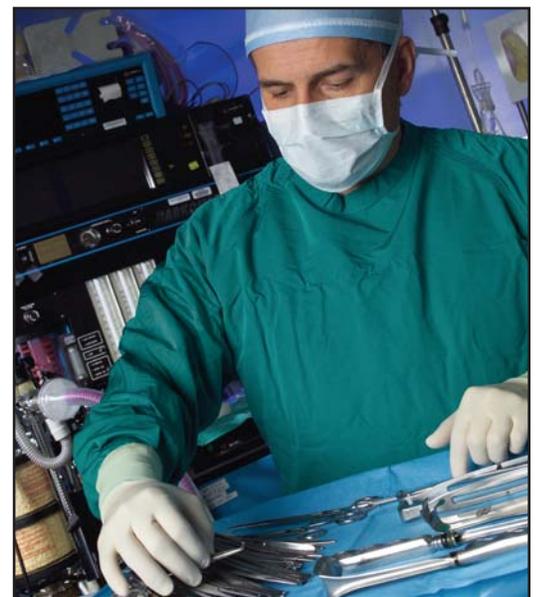
Today, according to the World Health Organization (WHO), a diabetes epidemic is underway, led by the United States. An estimated 30 million people worldwide had some form of diabetes in 1985 and, within 15 years the number had increased to 177 million. WHO projections suggest that the number of people suffering from diabetes will increase to some 370 million by 2030.<sup>1</sup>

Although significant attention and resources have been dedicated to the development of new treatments, there is

currently no artificial treatment that can maintain normal blood glucose levels at all times. The artificial pancreas does not yet exist. However, transplantation of functioning donor islets into type I diabetics offers a potential “cure” of diabetes by maintaining normal glucose levels at all hours, regardless of caloric intake.

### HOPE FOR TYPE I DIABETICS

Type I diabetics have suffered an autoimmune destruction of their beta cells within the pancreatic islets which renders them insulin deficient. Unlike type II diabetics, type I patients typically have normal sensitivity to insulin and, if



provided in appropriate physiologic amounts, insulin will cure diabetes. Current medical treatment of these patients requires frequent insulin injections of variable doses depending upon the calories ingested and the physical stress experienced. Research and clinical experience has now shown that transplanted islets in the form of a vascularized pancreas can provide a source of intrinsic insulin that is automatically regulated, creating a “cure” of the diabetic condition. This is done by maintaining normal glucose levels (euglycemia) and HbA1C (glycohemoglobin) values.

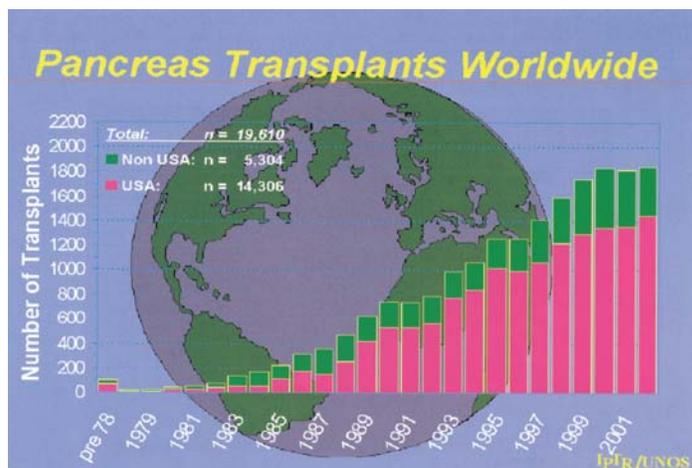
In contrast, the results of transplantation in the type II diabetic are disappointing. Since type II diabetics have varying degrees of insulin resistance, their inherent circulating insulin levels are typically elevated. Even though they may require insulin injections or medication to assist in controlling their sugars, transplanting pancreatic tissue rarely provides sufficient insulin to create a euglycemic condition. Transplantation is therefore not a consideration for these individuals outside of specialized, infrequent research protocols.

## THE HISTORY OF PANCREATIC TRANSPLANTS

The first pancreatic transplant was performed in December 1966 in combination with a cadaveric kidney transplant at the University of Minnesota by Drs. Lillihei and Kelly. This was done in an effort to treat an individual with type I diabetes and renal failure. Over the next seven years, 14 pancreatic transplants were performed with all but one failing within one year.<sup>2, 3</sup> Pancreatic transplantation remained a research treatment out of the mainstream until the late 1980s when physicians began to prescribe cyclosporin to prevent organ rejections. This greatly improved graft survivals and patient outcomes.



Figure A



Graph A

Since that time, the U.S. has seen a dramatic growth in the number of pancreatic transplant centers and patients treated.<sup>4</sup> (Graph A) The U.S. government recognized pancreatic transplantation as a mainstream therapy for type I diabetics in 1999 when Medicare approved coverage for eligible patients who have type I disease and native kidney failure. This coverage allows patients to receive a combined kidney and pancreas transplant or to receive a pancreas transplant after receiving a kidney transplant. Today, most insurance companies recognize these indications and some will even cover pancreatic transplantation in type I patients who still have adequate renal function yet suffer frequent hospitalizations or hypoglycemic unawareness despite excellent compliance.

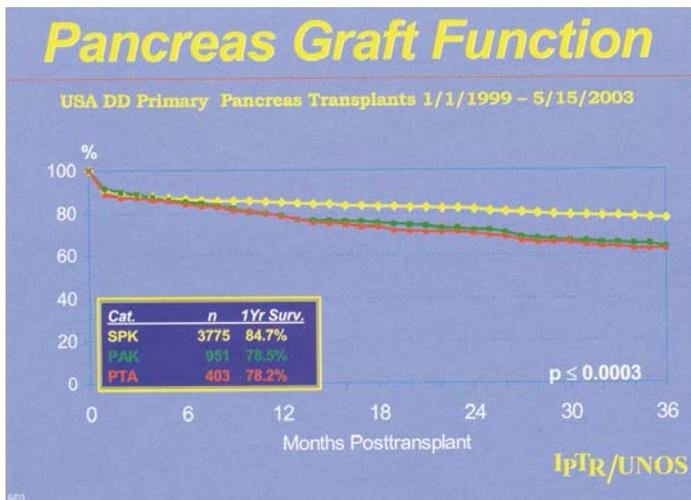
## THE PROCEDURE

Prior to implantation, a segment of the donor iliac artery is connected to the arteries of the pancreas (Figure A) to facilitate placement within the pelvis. The kidney and pancreas are then transplanted into the pelvis of the recipient. The arterial and venous blood supplies of the organs are connected to the patient’s iliac artery and vein. The transplant ureter is then connected to the bladder while the exocrine juice of the pancreas is drained into the GI tract<sup>5</sup> (Figure B). The surgery to place both organs typically takes five hours with a typical hospital stay of seven to 10 days.

## CANDIDATE CRITERIA

Optimal pancreas transplant candidates:

- are type I diabetics,
- suffer renal failure or have had a previous renal transplant,
- have good cardiac and physical reserve,



Graph B

- have an anticipated life expectancy of at least five years (typically younger than age 55),
- are compliant in managing their diabetes, and
- have no recent history of substance abuse, active infections or malignancy or major psychiatric illness which would interfere with their ability to give informed consent and participate in their long-term care.

Type I diabetics typically have had diabetes since childhood. Because the beta cells in the islets are destroyed, these patients require insulin from the time of diagnosis and cannot be maintained on oral agents. Confirmation of type I diabetes can be made by checking a C-peptide level in the patient's serum. Type I diabetics have an extremely low or undetectable C-peptide level compared to type II diabetics who usually have abnormally elevated values.

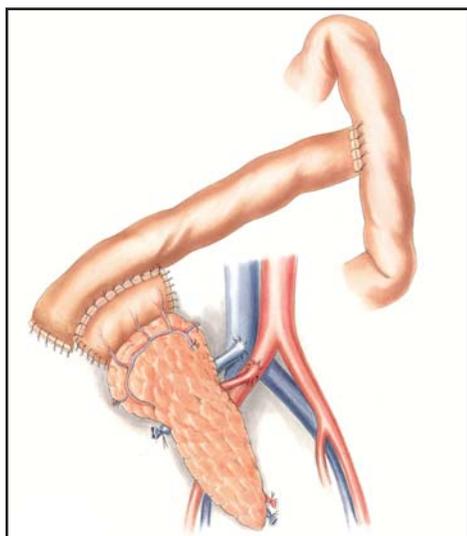
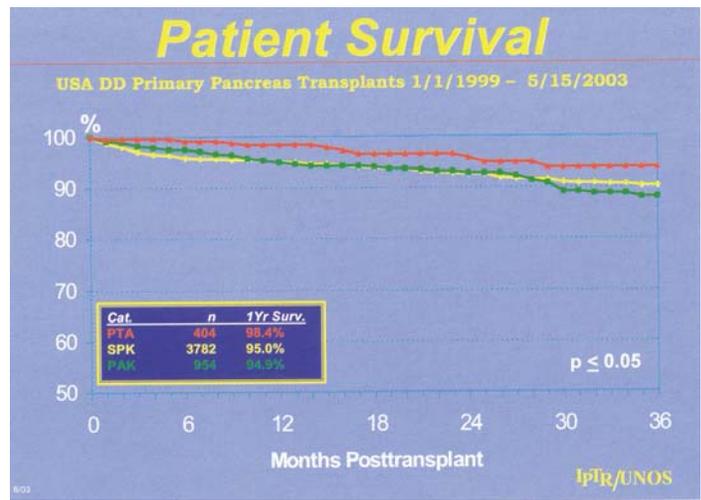


Figure B

Age is also an important factor. Type I diabetics significantly older than 55 are much more likely to suffer underlying coronary or cerebrovascular disease which may make the surgical risk prohibitive.



Graph C

## THE RESULTS

Both patient and pancreatic graft survivals have steadily improved over the past 15 years and within the last four years are now approaching renal allograft success rates. Pancreatic graft survival rates (insulin independence) for one year post-transplant has increased from 76 percent in 1992 to 85 percent in 2003.<sup>4</sup> (Graph B) Patient survival rates for one year post-transplant within the same time frame have increased from 91 percent to 95 percent.<sup>4</sup> (Graph C) Multiple reports document a stabilization of diabetic complications following successful transplantation including retinopathy, peripheral neuropathy, and even GI autonomic neuropathy to some degree. A report in the New England Journal of Medicine in July 1998 showed a reversal of diabetic nephropathic histologic lesions in patients with functioning pancreatic transplants after 10 years of follow-up. This was coupled with reduction of protein in the urine and improved creatinine clearances.<sup>6</sup> (Figure C)

TABLE 1. DEMOGRAPHIC CHARACTERISTICS AND MEASURES OF RENAL FUNCTION AT BASE LINE AND 1, 5, AND 10 YEARS AFTER PANCREAS TRANSPLANTATION IN PATIENTS WITH TYPE 1 DIABETES.

PATIENT NO. AND SEX	AGE AT BASE LINE	DURATION OF DIABETES AT BASE LINE	URINARY ALBUMIN EXCRETION			CREATININE CLEARANCE			
			BASE LINE	5 YR	10 YR	BASE LINE	1 YR	5 YR	10 YR
		yr	mg/24 hr			ml/min/1.73 m <sup>2</sup>			
1/M	33	20	7	2	6	138	75	82	83
2/F	31	15	8	4	23	113	71	63	68
3/F	33	24	12	21	43	101	61	86	91
4/F	35	22	86	6	6	116	86	91	78
5/M	30	23	120	80	48	128	61	90	89
6/F	33	17	127	155	18	84	49	44	50
7/F	31	27	278	126	20	110	54	72	67
8/F	38	29	1276	40	176	78	65	68	67
Mean ±SD	33±3	22±5	103*	30*†	20*‡	108±20	65±12§	74±16§	74±14§

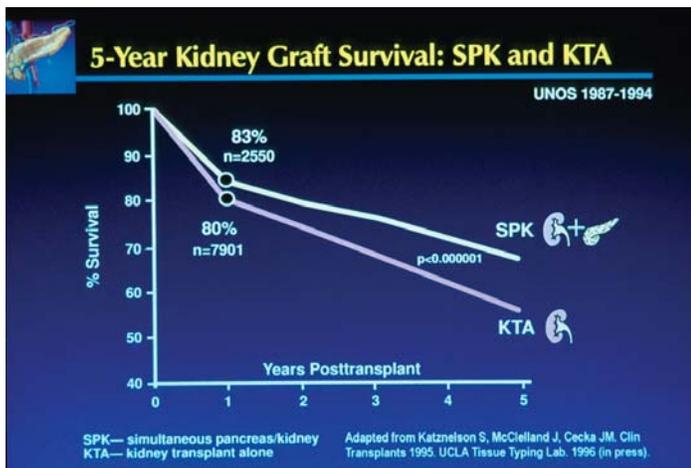
\* Values shown are medians. The values for albumin excretion were not normally distributed and were therefore logarithmically transformed for statistical analysis.

†P=0.07 for the comparison with the base-line value.

‡P=0.11 for the comparison with the base-line value.

§P<0.001 for the comparison with the base-line value.

Figure C



Graph D

Renal benefit results in improved kidney function and longevity in the diabetic patient. Even prior to 1992, adding a pancreas to the kidney transplant improved long-term renal success.<sup>7</sup> (Graph D) This protection remains an important benefit of pancreatic transplants today.

## REFERRING TO OU PHYSICIANS TRANSPLANT TEAM

Type I diabetic patients who might benefit from transplantation are usually referred to the OU Physicians Transplant team by their primary care physicians, nephrologists or endocrinologists. Once a referral is made, the patient's transplant coordinator arranges all appointments, tests and evaluations. The patient is evaluated by several members of our transplant team including a transplant physician, transplant surgeon, transplant coordinator, financial counselor and social

worker. The results of these evaluations are then brought to a committee who will review them and determine transplant candidacy. This process typically requires two to three months to complete. **Referrals can be made by calling the transplant center directly at 405-271-7498 or toll-free at 877-817-6911, ext.7498.**

## References

1. Dave Joffe, Editor-in-Chief, Items for the Week: Diabetes Set to Increase from 177 to 370 Million by 2030, Diabetes in Control.com, Issue 257, April 27, 2005. (<http://www.diabetesincontrol.com/modules.php?name=News&file=article&sid=2684>)
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