PANCREAS TRANSPLANT: AN OPTION FOR TREATMENT OF INSULIN DEPENDENT DIABETES MELLITUS

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A manuscript submitted in partial fulfillment of the requirements for the degree of

MASTER OF NURSING

WASHINGTON STATE UNIVERSITY
Department of Nursing

December 2000
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ACKNOWLEDGEMENT

I am grateful for the assistance and encouragement of my family, friends, co-workers, classmates and faculty that enabled me to reach my goal.
ABSTRACT

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The syndrome of Type 1 diabetes mellitus includes abnormal blood glucose metabolism and is associated with development of retinopathy, nephropathy and neuropathy. Type 1 diabetes is an autoimmune disease that destroys the beta cells in the islet of Langerhans in the pancreas. It is a catabolic disorder in which circulating insulin is absent and external replacement is required. The DCCT Research (1993) Group proved the value of a rigid schedule of insulin injections to reduce the development of complications. Pancreas islet cell transplantation and whole-organ pancreas transplant are surgical options that may cure Type 1 diabetes. This paper reviews the mechanism of end organ damage caused by the hyperglycemia of Type 1 diabetes, current medical and surgical therapy and describes patient eligibility criteria for transplant for use by the primary care provider.
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DEDICATION

This paper is lovingly dedicated to my son Thomas
who inspires me
to try harder each day.
INTRODUCTION

Diabetes afflicts approximately 6% of the general population and is currently the third most common disease and the fourth leading cause of death by disease in the United States (Harris, Hadden, Knowles & Bennett 1987; Libman, Songer & Laporte 1993). Of the estimated 16 million diabetic Americans, 4 million take insulin, and 1 million have insulin dependent diabetes mellitus (Type 1), juvenile onset. The syndrome of Type 1 diabetes includes abnormal blood glucose metabolism with complications such as retinopathy, nephropathy and neuropathy. Diabetes is the leading cause of renal failure and blindness, as well as the number one disease cause of amputation and impotence (Stratta et al, 1997). Diabetes is associated with accelerated atherosclerosis, abnormal lipid metabolism, and cardiovascular disease (Nathan, 1993). The prevalence of hypertension among the diabetic population is double the general population (Bucala, Cerami & Vlassara, 1995). For this reason, compliance with medical therapy is important to delay complications of diabetes.

Surgical therapy should be considered when a diabetic has frequent acute complications (hypoglycemia, hyperglycemia and ketoacidosis), problems with medical therapy that have become incapacitating and consistent failure of insulin therapy to prevent acute complications (ADA, 2000).

DISEASE PROCESS: INSULIN DEPENDENT DIABETES MELLITUS

Diabetes is a disease of the pancreas. Specifically, insulin dependent (Type 1) diabetes is an autoimmune disease where the beta cells within the islet of Langerhans in the pancreas are selectively destroyed (Tyden, Reinholt, Sundkvist & Bolinder, 1996). The destructive process is detectable by the islet cell antibody test, to confirm the autoimmune process and developing disease. The anti-insulin antibodies that destroy the beta cells are present for several years before symptoms occur (Saudek, Rubin & Shump, 1997). Most islet cell antibodies are directed against an enzyme localized in the
pancreatic beta cells. Immunoassay kits are available to test siblings of affected children with Type 1 diabetes and adults with atypical symptomatology of non-insulin dependent diabetes mellitus (Type 2) (Karam, 2000).

Type 1 diabetes occurs most commonly in juveniles, and occasionally in adults, particularly the nonobese and those who are elderly when hyperglycemia is first noted. It is a catabolic disorder in which circulating insulin is essentially absent, plasma glucagon is elevated and the beta cells are non-responsive to insulinogenic stimuli. Treatment is exogenous insulin to reverse the catabolic state, prevent ketosis, reduce hyperglucagonemia, and reduce elevate blood glucose (Karam, 2000).

PATHOPHYSIOLOGY OF MICROVASCULAR DAMAGE

The association of microvascular disease and neuropathy with diabetes and the relation of these complications to the duration of diabetes suggest that they result from hyperglycemia. Tissues affected by diabetes (the retina, the kidney, and the nerves) are freely permeable to glucose (Clark, 1995).

There are broad categories by which complications are categorized: glucose-related (abnormal metabolism and excessive glycation of circulating and membrane-bound proteins) and vascular mechanisms (alterations in the endothelium and supporting cells, hyperfiltration and intrarenal hypertension). Other mechanisms include alterations in platelet function, growth factors and genetic influences (Nathan, 1993).

Chronic hyperglycemia is measured with HgA1c (glycosylated hemoglobin) testing, which demonstrates metabolic control. HgA1c is produced by nonenzymatic condensation of glucose molecules with free amino groups on the globin part of the hemoglobin molecule. The combined product is normally only 4-7% of the total hemoglobin that circulates in the red blood cells whose life span lasts up to 120 days, reflecting the level of glycemia over the preceding 8-12 weeks (Karam, 1998).
Glucose molecules adhere to the hemoglobin (hgb) molecules in the red blood cells, while they circulate for their life span of about four months. During hyperglycemia, more hgb is glycated (glucose molecules attached to a protein, in this case hemoglobin), increasing the HgA1c (Saudek, Rubin & Shump, 1997).

Persistent hyperglycemia over time increases the levels of nonenzymatic glycosylation products in the blood and tissues, resulting in basement membrane thickening and microangiopathy. Late products of nonenzymatic glycosylation are termed advanced glycosylation products (AGEs), and contribute to many of the long term complications of diabetes (Bucala et al., 1995).

AGEs alter the structural and functional properties of proteins by cross-linking amino groups with each other. The cross-linking of the connective tissue collagen contributes to the vascular and ligament rigidity that occurs with normal aging, but is accelerated in diabetics. Collagen-linked AGEs also act as reactive foci to covalently trap circulating serum proteins such as albumin, lipoproteins and immunoglobulins. This effect may contribute significantly to the increase in protein deposition and in basement membrane thickening that occurs in the renal vasculature. Cell surface receptors that are specific for the recognition, uptake and degradation of AGE-modified proteins have been identified on circulating monocytes, endothelial cells and renal mesangial cells. AGEs are chemotactic for monocytes and the cell surface receptor uptake of AGE-modified proteins initiates cytokine-mediated processes that promote tissue remodeling. Occupancy of endothelial cell receptors by AGEs leads to increased vascular permeability, downregulation of the cell surface anticoagulant thrombomodulin, and increased synthesis of the procoagulant tissue factor. Renal mesangial cells respond to AGEs by increasing the production of extracellular matrix proteins. These diverse receptor-mediated effects amplify the host response to advanced glycosylation and play an important role in the ultimate vascular and renal toxicity of AGEs (Bucala et al., 1995).
Abnormalities in vascular tone and regional blood flow contribute to tissue hypoperfusion, end-organ hypoxia and cardiovascular complications. Nitric oxide (an endothelium-derived vascular smooth muscle relaxing factor) is chemically inactivated by collagen bound AGE moieties. Nitric oxide is necessary for the maintenance of normal vascular tone and blood pressure, so inactivation by vascular wall AGEs may explain the progressive impairment in endothelium dependent (nitric-oxide mediated) responses that occur in the coronary and systemic circulation of diabetics (Bucala et al., 1995).

Biochemical modifications that affect the functional integrity of low-density lipoproteins (LDL) are among the pathological processes that are thought to be central in the development of atherosclerosis. LDL is the major lipoprotein responsible for transferring both exogenously absorbed and endogenously synthesized lipids to peripheral tissues. A dyslipidemia characterized by increased levels of LDL, very-low density lipoproteins (VLDL) and intermediate density lipoproteins (IDL) is commonly found in diabetic patients and increases their risk for myocardial infarction and cerebral vascular attack (Bucala et al., 1995). Therefore, treatment options must focus on maintaining tight control over these variables or curing the disease.

TREATMENT OPTIONS

Medical Therapy

The Diabetes Control and Complications Trial (DCCT) demonstrated the value of tight glucose control to slow the progression of diabetic complications in patients with Type 1 diabetes (The DCCT Research Group, 1993). Tight blood glucose control reduces the incidence and severity of diabetic complications, but requires an increased frequency of insulin injections and increases the risk of hypoglycemic episodes. The regimen also requires finger stick blood glucose measurements 3-4 times per day and multiple insulin injections. This daily regimen improved the mean HgA1c to only
one gram above normal (4-7%) (DCCT Research Group, 1993). A relative decrease of 30-60% in the clinical manifestations of retinopathy, nephropathy and neuropathy was observed when intensively treated patients were compared with the conventionally treated group (Bucala et al., 1995). However, some patients continue to have extreme oscillations of blood glucose, even with tight control, while others develop complications when their HgA1c is only moderately elevated (Sutherland & Gruessner, 1997).

Hemodialysis has been shown to be relatively ineffective for removing advanced glycosylation end products (AGEs) from the serum of patients with end-stage renal disease (ESRD). Specifically, in diabetic patients undergoing high-flux, conventional or chronic peritoneal dialysis, AGEs levels persist at a level 3.5 to 6 times higher than normal. High-flux hemodialysis was shown to reduce AGEs levels in both diabetic and non-diabetic patients, but returned to previous high levels 3 hours after treatment. Circulating AGEs accumulate under conditions of renal compromise and are refractory to removal by currently available dialysis therapies. AGE levels decreased and remained within normal limits in ESRD patients who underwent renal transplantation (Bucala et al., 1995).

A small nucleophilic compound that possesses a terminal amino group named aminoguanidine, reacts effectively with glucose-derived reactive intermediates before protein-protein or protein-lipid cross links form. Aminoguanidine has been studied in experimental animals, since 1986. It has been reported to inhibit glucose-mediated cross-linking, and consequently tissue damage. More specifically, aminoguanidine has been demonstrated to decrease AGE accumulation and protein trapping in the glomerular basement membrane of the kidney, delaying the onset of vasodilatory abnormalities, retinal vascular lesions and improves diabetic neuropathy (Bucala et al., 1995). Aminoguanidine, as a drug for treatment in humans, is currently in Phase 3 clinical studies and yet to be proven as an effective agent. (J.Powers, FDA CDER Drug
Exogenous insulin regimens do not achieve the glucose metabolism of a normally functioning endogenous insulin source. The pancreas can provide moment to moment insulin secretion in response to changing blood glucose levels that may be necessary to fully protect against the development of long-term microvascular complications (Robertson, 1992). Despite intensive insulin therapy, variability in the blood glucose levels of diabetic patients do not match the precisely controlled levels achieved in individuals with normally functioning pancreatic islets (Bucala et al., 1995).

Islet Cell Transplant

Pancreas islet cell transplantation has been explored as a treatment option for IDDM. It requires immunosuppression but is not a major surgery. However, of the more than 200 islet allografts performed in the 1990’s less than 10% achieved insulin-independence after one year. Clinical trials continue, but are limited to patients who accept a low probability of success, or in whom the surgical risks of whole organ pancreas transplant are too risky (Sutherland & Gruessner, 1997). Intra-portal pancreatic-islet cell transplant is minimally invasive and can be repeated if the first graft is rejected (Luzi, 1998). Islet cell transplantation is performed via percutaneous transhepatic catherization (without significant acute or long term effect on liver function or portal venous pressure), or through a mesenteric catheter (placed during laparotomy) that was exteriorized and the patency maintained for 12-14 days with diluted heparin infusion. The islet cells are then infused over a 30-minute period on 1-3 occasions, depending on the number of donor cells determined necessary for that patient (based on body weight). Islet cell transplantation has not been as successful as whole organ pancreatic transplants in achieving insulin independence. Actually, many patients have acquired symptoms of adult-onset diabetes, requiring small amounts of insulin to maintain stable glucose levels. One study showed that islet cell
transplantation (versus whole organ) results in endogenous insulin secretion over at least 6 years and near normalization of glucose metabolism, with the addition of small amounts of exogenous insulin. At present, treatment strategies involving islet cell transplantation can offer good glucose control and prevention of long-term complications, with less hypoglycemia (Alejandro et al, 1997).

Pancreas Transplant

Pancreas (whole-organ) transplantation is the only current treatment of IDDM that consistently establishes an insulin-independent, normoglycemic state (Sutherland, 1997). Pancreas transplantation is performed in patients with uremia and diabetes, concurrently or after kidney transplant. Pancreatic grafts generally come from cadaveric donors. Pancreatic graft drainage is venous and empties into the systemic circulation instead of the portal system. Exocrine secretions from the grafted pancreas usually drain into the urinary bladder, allowing for post-operative detections of decreases in urinary amylase levels, an indicator of graft rejection (Robertson, 1992).

Anti-T cell antibodies are used to induce immunosuppression pre-operatively, then cyclosporin, azathioprine and prednisone are used to maintain immunosuppression in the postoperative period (Robertson, 1992). Pancreas transplantation reverses the lesions of diabetic nephropathy in Type 1 diabetics without uremia and who are normoglycemic after transplantation (Fioretto, Steffes, Sutherland, Goetz & Mauer, 1998).

Simultaneous pancreas and kidney transplantation was done for the first time in 1966 in an insulin dependent diabetic with end-stage renal failure, in an attempt to achieve normal metabolic balance and stop progression of diabetic complications (Robertson, 1992). In the U.S. from October 1987 to November 1996, transplants associated with diabetes included 4,300 simultaneous pancreas-kidney (SPK) transplants, 390 pancreas after kidney (PAK) transplants and 240 pancreas (PTx)
transplants, as reported to the United Network for Organ Sharing. Patient survival rates, for the 9-year period at 1 and 3 years were 92% and 86%, respectively. These rates were similar in all transplant categories (Sutherland & Gruessner, 1997).

Vascular pancreas transplantation (PTx) is the treatment of choice for uremic insulin dependent diabetic patients, because it cures the uremia and provides an endogenous source of insulin (Balsells, 1998). Pancreas transplants are now performed as a routine for uremic diabetic recipients of renal transplants, either simultaneously or after the renal transplant. The American Diabetes Association (1992, 2000) recommends PTx as an acceptable therapeutic alternative to prolonged insulin therapy in patients with IDDM and renal failure, who have had or plan to have a kidney transplant. In addition, it recommends that PTx be an option for Type 1 diabetes patients with either glucose hyperlability, or hypoglycemia unawareness that significantly impairs quality of life (ADA, 1992). Also, PTx may be an effective treatment for the patient beginning to have early diabetic complications (Stratta et al, 1997).

PATIENT PROFILE

Every provider has cared for a patient whose labile glucose levels defy explanation and treatment modalities. Many of these patients are identified as “brittle”; which is defined by recurrent episodes of hypoglycemia and hyperglycemia that disrupt daily life. A progressive review of daily management can help balance blood glucose levels; timing of insulin injections in relation to meals, correcting faulty injection technique (i.e. avoidance of injecting into lipohypertrophic areas which can produce erratic insulin absorption) or assessment of exercise and meal scheduling. The total daily dose of insulin is 0.5-1.0 U/kg for most diabetics. Nocturnal hypoglycemia is especially common when there is hypoglycemic unawareness, and may result in erratic sugar levels the following day. Other causes for lability include psychological difficulties, gastroparesis, Addison’s disease and celiac disease (Ryan, 1998).
When intensive medical treatment is not effective, surgery may be an option. All patients undergo comprehensive pretransplant medical evaluation, listed in Table 1. The examinations are tailored to the individual, based on presence of specific signs and symptoms. Included in the work-up are confirmation of the presence of IDDM, the patient's operative risk, and documented end-organ complications. Specific criteria for transplantation are listed in Table 2. The major determinations for recipient selection are degree of nephropathy, cardiovascular risk, and diabetic complications. Renal dysfunction is measured to determine if the patient needs a combined pancreas-kidney, or pancreas-only transplant. If the patient had intermediate renal function (creatinine clearance 45-70 ml/min or severe proteinuria), then oral cyclosporin testing is completed to assess renal functional reserve for postoperative immunosuppression (Stratta et al., 1994).

DIAGNOSTIC TESTING

Patient preparation and selection criteria is described in detail by Stratta et al. (1994). All patients considering pancreas transplant require an extensive medical examination, outlined in Table 1. Each evaluation is individually tailored, depending on the need to evaluate specific symptoms of health problems. In detail, each patient's work-up includes: confirmation of the diagnosis of insulin dependent diabetes, absence of exclusion criteria and presence of end-organ complications of diabetes. If a patient is a probable candidate, further evaluation (Table 2) by a multidisciplinary team is used to determine the type and timing of the procedure.

The primary symptoms for recipient selection are the degree of nephropathy, presence of diabetic complications and cardiovascular risk. Patients are advised about pancreas only transplant (PTx) versus combined pancreas-kidney transplantation (PKT) based on their degree of renal dysfunction. In addition, patients with intermediate renal dysfunction (creatinine clearance > 70ml/min) undergo an oral cyclosporine
challenge test to assess renal functional reserve.

The cardiovascular work-up is used to determine surgical risk. If history, physical exam or non invasive cardiac studies are abnormal, then cardiac angiography is performed. Criteria for cardiac catheterization are: age > 45 yrs, diabetes for > 25 yrs, smoking, longstanding hypertension, previous major amputation due to peripheral vascular disease or history of a stroke. Previous myocardial infarction, angioplasty or coronary bypass grafting are not necessarily exclusion criteria. Specific criteria for inclusion and exclusion are listed in Table 2. Major criteria for solitary pancreas transplant are: presence of two or more long-term diabetic complications, glucose hyperlability with hypoglycemic unawareness, impaired quality of life and adequate renal functional reserve (Stratta et al., 1994).

BENEFITS AND RISKS

The benefits of pancreas transplant are many. Pancreas transplantation is superior to intensive insulin treatment for balanced glucose control and prevention of long-term complications. The mean HgA1c levels in patients with transplants 5 and 10 years after transplantation were 5.3% and 5.5%, respectively. That is below the target value of 6% described by the DCCT Research group. This comparison suggests that pancreas transplant is superior to intensive insulin treatment (three or more daily insulin injections or use of an insulin pump) for metabolic control. Transplanted beta cells secrete insulin in response to the ambient glucose concentration through a closed-loop, feedback-regulated mechanism that limits the diurnal plasma glucose fluctuations that occur with exogenous insulin administration (Luzi, 1998). Successful transplantation of the pancreas (in combination with a kidney or alone) normalized glucose metabolism in Type 1 patients, but the effect of the graft on long-term complications varies (Remuzii, Ruggenenti & Mauer, 1994). It has been found that nephropathy symptoms improve, but not diabetic retinopathy. This probably is due to
the late restoration of beta cell function, after proliferative retinal disease is established (Luzi, 1998).

After transplantation glucose control is excellent, with normal (4 -7%) HgA1c levels being reported in patients with functioning grafts, and no hypoglycemia (Ryan, 1998). Several studies have followed groups of post-transplant patients and evaluated their results. Results documented by Balsells, et al, in 1998 found that more than 80% of the insulin-independent patients with both (kidney and pancreas) grafts functioning had normal oral glucose tolerance tests 1 year after surgery. This proportion remained stable throughout the study (mean time 4.2 +/- 2.3 years), remaining at 80% after 6 years from transplantation. The same group had normal HgA1c levels throughout the follow-up period (Balsells et al., 1998).

Since 1997, more than 1,000 pancreatic transplants per year in the United States have been performed. Ninety percent of these transplants were combined with kidney transplants, and have a 1 year graft survival rate of more than 80%. Kidney survival is unaffected or improved by simultaneous pancreas transplantation, but the graft survival rate for pancreas after kidney transplants was somewhat lower (Sutherland and Gruessner, 1997).

It has been previously shown that preemptive pancreas transplant can be performed safely in the absence of uremia, development of end-stage renal disease, potentially arresting the progression of diabetic complications. Further, one could speculate that pancreas transplant could be performed before the development of advanced diabetic complications or the need for kidney transplant. There are no reliable markers to predict which diabetic patients will have severe end-organ complications (Nathan, 1993). Fioretto (1998) concluded that pancreas transplantation can reverse lesions of diabetic nephropathy by decreasing the thickness in the glomerular and tubular basement membranes, but that it takes more than 5 yrs of normoglycemia.
Solitary pancreas transplant is restricted by necessity to patients who already have demonstrated early diabetic complications, because risks seem to be higher for solitary pancreas transplant versus combination pancreas-kidney procedure. Pancreas only transplants are associated with a higher risk of thrombosis and organ rejection (Stratta et al., 1995). Complications are managed with anticoagulation therapy and monitoring of urine cytology, serum and urine analysis, serum anodal antitrypsinogen, and protocol pancreas allograft biopsies (Stratta et al., 1995).

Pancreas transplantation is an invasive procedure with perioperative and postoperative morbidity. The rejection rate is higher than for combined pancreas-kidney transplant. Lifelong immunosuppression is associated with renal toxicity and increased risk of infection and cancer (Luzi, 1998).

COSTS

As reported by Stratta et al., in 1995, the mean waiting time for a transplant patient was 2.3 months, with a range of 2-10 months. The average length of hospital stay is over 16 days, and the hospital charges are over $100,000. A detailed list of published expenses are presented in Table 3.

CONCLUSION

Pancreas transplant has become increasingly important in the treatment of Type 1 diabetes mellitus. Position statements have been issued from the American Diabetes Association, the American Society of Transplant Surgeons, and the American Society of American Transplant Physicians that recommend the pancreas transplant be considered an alternate therapy for diabetics in renal failure, who have already had or are considering renal transplant (Stratta et al., 1997).

Transplantation can improve quality of life, and the hope is that it will prevent long-term complications of diabetes. Problems include: risks of a surgical procedure
(8% required a second surgical procedure), lifelong immunosuppression, a 2-3% risk of immunosuppression induced lymphoma and osteoporosis caused by steroids (Ryan, 1998). Cyclosporin, used to prevent transplant graft rejection, causes lesions in the kidney whether it is native or transplanted (Luzi, 1998). For most diabetics, even those with complications, current standard medical therapy is safer than transplantation. For a patient without severe renal disease or labile glucose control that is disruptive and dangerous, the 10% mortality and 20% graft failure risks may not be decisive. As always, the patient should be well informed of all potential risks and benefits, so that they may be prepared to take part in the decision process (Ryan, 1998).

There are 124 pancreas transplant centers in the United States, and the total number of transplants in 1997 was 1,045. The overall 1-year patient survival is 91%, and the 1-year transplant survival (completely insulin-independent) is 75% (Stratta, 1998). Pancreas transplantation should be a therapeutic alternative to insulin therapy in diabetics with imminent or established renal disease who have had or plan to undergo renal transplant. The additional transplantation of the pancreas does not alter patient survival, may improve kidney survival, restores normoglycemia, reverses most complications of diabetes and can be done simultaneously to improve pancreas transplant success (ADA, 2000).
REFERENCE LIST


### TABLE 1
**PANCREAS TRANSPLANT EVALUATION**

I. Interviews and consults
   - A. History and physical examination by nephrologist, endocrinologist and transplant surgeon
   - B. Ophthalmology evaluation including visual acuity, fluorescein angiography, retinal fundus photography with retinopathy score and slit-lamp examination
   - C. Transplant coordinator and medical social worker interview, including completion of quality of life questionnaire
   - D. Gynecological consultation for women (pelvic exam with pap smear)
   - E. Dental evaluation
   - F. When indicated, additional evaluations may be required by orthopedic surgery, podiatry, psychiatry, neurology or gastroenterology.

II. Cardiovascular, respiratory, and peripheral vascular evaluations
   - A. Standard testing includes orthostatic vital signs, 12-lead echocardiogram, chest x-ray, and exercise treadmill or stress thallium study
   - B. Additional studies may include arterial blood gases, echocardiography, autonomic/peripheral vasomotor reflexes, Doppler arterial studies, ankle/brachial index, transcutaneous oxygen monitoring, plethysmography, carotid Doppler examination, aortography with run-off, or pulmonary function tests, as indicated
   - C. Cardiology consultation with or without coronary angiography, as indicated

III. Metabolic and endocrine evaluation
   - A. Standard testing includes fasting blood glucose, glycohemoglobin, and fasting lipid panel (cholesterol, triglycerides and HDL-cholesterol)
B. Fasting and stimulated C-peptide levels are used to assess type of diabetes, if needed

IV. Genitourinary/renal evaluation

A. Standard testing includes electrolytes, BUN, creatinine, urinalysis with culture, 24-hr urine for protein and creatinine clearance, voiding urethrocystourethrogram with post-void residual, and radiometric glomerular filtration rate

B. In addition, kidney biopsy, or evaluation of erectile dysfunction may be indicated

C. Cyclosporine challenge test when indicated

V. Serology and immunology evaluation

A. ABO blood type and HLA tissue type

B. Cytotoxic antibodies

C. Viral titers (Epstein Barr virus, Herpes simplex virus, Varicella-Zoster virus, HIV, hepatitis-B virus, hepatitis-C virus and cytomegalovirus)

D. VDRL/FTA

VI. Other laboratory tests

A. CBC with differential and platelets, PT, PTT, chemistry profile, amylase, lipase

B. Abdominal ultrasound of kidneys and bladder

C. Mammography in females over 35 yrs

D. Hemoccult X3

E. When indicated, nerve conduction studies, gastric emptying studies, electromyography

Source: Stratta et al., 1994.
TABLE 2
CRITERIA FOR PANCREAS TRANSPLANTATION

I. Exclusion criteria

A. Insufficient cardiovascular reserve: (1) Coronary angiographic evidence of significant non-correctable coronary artery disease; or (2) ejection fraction below 50%; or (3) recent myocardial infarction

B. Ongoing substance abuse (drug or alcohol)

C. Major ongoing psychiatric illness

D. Significant history of non-compliance

E. Lack of well-defined diabetic complications

F. Extreme obesity (>50% ideal body weight)

H. Inability to understand the nature of pancreas transplantation

II. Inclusion criteria

A. Presence of Type I diabetes mellitus (documented by metabolic testing when indicated)

B. Ability to tolerate surgery and immunosuppression (as assessed by pretransplant medical evaluation)

C. Emotional and socio-psychological suitability

D. Able to understand therapeutic nature

E. Presence of secondary diabetic complications

F. Financial resources

III. Specific entry criteria for pancreas transplant alone

A. Diabetic nephropathy: creatinine clearance below 40 ml/min

B. Dialysis-dependent
IV. Specific entry criteria for pancreas transplant alone

A. The presence of two or more diabetic complications defined as:
   1. Proliferative retinopathy
   2. Early nephropathy with a creatinine clearance > 70 ml/min and proteinuria > 150 mg/24 hr but < 3 g/24 hr
   3. The presence of overt peripheral or autonomic neuropathy
   4. Vasculopathy with accelerated atherosclerosis or

B. The presence of hyperlabile diabetes as defined by an adverse event scoring system which takes into account the frequency and severity of episodes of ketoacidosis, hypoglycemia, infections, and impairment of quality of life

C. Creatinine clearance above 55 mg/min and serum creatinine below 2.0 mg/dl after cyclosporine challenge test

Source: Stratta et al., 1994
TABLE 3
COSTS FROM 1998

-Amputation:
  toes: $778-916
  above the knee: $1835-2159
  below the knee: $1640-1935

-Pancreatectomy (total or subtotal w/ autologus transplant on whole organ or pancreatic islet cells): $7800-9500

-Donor Pancreatectomy (with preparation and maintenance of allograft from cadaver donor with or without duodenal segment for transplant): fee range not well established.

-Transplant of pancreatic allograft: fee range not well established, expect $4400-5750.

-Renal transplant
  donor nephrectomy with prep and maintenance of allograft from cadaver: $2365-2820.
  from living donor: $3805-4510.
  recipient nephrectomy: $2310-2760.
  renal allotransplant, implantation or graft (excluding donor or recipient nephrectomy): $4545-5435.
  renal allotransplant (with recipient nephrectomy): $5630-6705.

-Test for penile tumescence for evaluation of impotence: $182-214
  If this test is not related to insulin dependent diabetes, it may be deemed medically unnecessary and not paid by Medicare.

- Barium swallow, air contrast with barium for evaluation of gastroparesis: $187-223
- Twelve lead electrocardiogram (ECG), with interpretation and report: $56-67.
- Cardiac stress test, with treadmill or bicycle, continuous ECG, with or without pharmacological stress, with MD supervision, including interpretation and report: $249-305.
- Electromyograph (EMG), for diagnosis of paresthesia:
  2 extremities: $247-296.
  4 extremities: $408-489.
- Sensory function testing: $71-85.
- Fundus photography, with interpretation and report: $59-70.

Lab:
- Insulin induced C-peptide suppression panel (to confirm beta cell function):
  $320-435.
- Urinalysis: $15-20.
- Creatinine clearance: $28-35.
- C-reactive protein: $26-32.

- End-stage Renal Disease related services for one month for patients over 20 yrs old: $355-430.