Pancreatic Transplant vs. Islet Cell Transplant
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Grand Rounds
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UCHSC
Disclosure

✓ No disclosures
Type 1 Diabetes

- Risk is from total lifetime exposure to elevated glucose
- Diabetes Control and Complications Trial - near perfect control of glycemia can be obtained with medical therapy but is unrealistic in clinical practice
- This tight control also increases the risk of severe hypoglycemia

Type 1 Diabetes

• The only way to restore normoglycemia without associated hypoglycemia is by replacing the pancreatic islet B-cells

• This can be done by:
  1. transplantation of a vascularized pancreas
  2. infusion of isolated pancreatic islets
Pancreas Transplant

- 1st – 1966
- Simultaneously with kidney
- University of Minnesota
- 2004 – > 17,000 pancreatic recipients in US

- Kelly et al. Allotransplantation of the Pancreas and doudenum along with the kidney in diabetic nephropathy. Surgery. 1967
- Sutherland et al. Lessons learned from more than 1000 pancreas transplants at a single institution. Ann Surg. 2001
Pancreas Transplant

- Total: $n = 23,056$
- Non USA: $n = 5,924$
- USA: $n = 17,132$

Number of transplants over years:
- 1978: 1
- 1979: 10
- 1980: 100
- 1981: 200
- 1982: 300
- 1983: 400
- 1984: 500
- 1985: 600
- 1986: 700
- 1987: 800
- 1988: 900
- 1989: 1,000
- 1990: 1,100
- 1991: 1,200
- 1992: 1,300
- 1993: 1,400
- 1994: 1,500
- 1995: 1,600
- 1996: 1,700
- 1997: 1,800
- 1998: 1,900
- 1999: 2,000
- 2000: 2,100
- 2001: 2,200
- 2002: 2,300
- 2003: 2,400

Map showing number of transplants worldwide:
- USA: 17,399
- Non USA: 5,924
- Other: 2,526
Recipient Categories

1. Uremic patients with diabetes who receive a simultaneous pancreas and kidney (SPK) transplant
2. Pancreas after kidney transplant (PAK) in nephropathic patients who already have had renal insufficiency corrected (live donor kidney transplant)
3. Pancreas transplant alone (PTA) in nonuremic recipients

Gruessner et al. Pancreas transplant outcomes for US and non-US cases as reported to UNOS and the IPTR as of 2002. UCLA.

• 5700 Pancreas transplants
  - SPK >4000
  - PAK >1300 (this is increasing because of live donors)
  - PTA >460


<table>
<thead>
<tr>
<th></th>
<th>PT survival</th>
<th>Graft survival* (1yr)</th>
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</thead>
<tbody>
<tr>
<td>SPK</td>
<td>95</td>
<td>84.7</td>
</tr>
<tr>
<td>PAK</td>
<td>95</td>
<td>78.5</td>
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<tr>
<td>PTA</td>
<td>98</td>
<td>78.2</td>
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</tbody>
</table>

*graft survival = recipients were insulin independent

Outcomes at 5yrs 1998/99

Graft survival 5yrs
SPK 69%
PAK 58%
PTA 58%

Gruessner et al. Pancreas transplant outcomes for US. Clinical Transplant. 2004
Difference in graft survival

- Theory
  The SPK has a higher graft survival because we can monitor rejection of the pancreas in SPK transplants through the kidney.
  Rise in serum creatinine is a very sensitive indicator and available test for kidney rejection – no comparable test for the pancreas alone.

Donor Operation

Sabiston Textbook of Surgery, 17th ed. 2004
Back table preparation: Pancreaticoduodenal allograft

- Spleen is used as a handle (then removed)
- Arterial extension Y graft
- External iliac to SMA
- Internal iliac to splenic artery

Sabiston Textbook of Surgery, 17th ed. 2004
Bladder vs Enteric Drainage

- Exocrine secretion drained to A. bladder B. small intestine
- R side arterial/venous anastomosis because of the sigmoid colon
Most common
Pancreas on right
Kidney on left
Enteric drainage
Venous drainage into portal system (or iliac drainage)

Islet Transplant

• 1977 – in diabetic that already had kidney transplant
• 1990-2000 – 355 allo-islet transplant performed

At 1 year – 11% patients were insulin independent

Shapiro et al. NJM 2000

- Edmonton, Canada
- Changed the protocol
- 7 of 7 patients with T1DM receiving islet cell transplant had >1yr insulin independence
- Each Pt needed 2-3 separate transplants from 2-4 cadaveric donors to achieve the adequate mass
Edmonton Protocol

- Excluded donors >50yrs
- Reducing ischemic injury during pancreas storage
- Avoiding islet-toxic reagents during islet processing
- Culturing islet cells to allow pre-transplant initiation of immunosuppression (2 days)
- Avoiding glucocorticoids and minimizing calcineurin inhibitors
Ryan et al. Diabetes. 2005

- 5 year follow up of Edmonton Protocol
- 65 Pts received islet cell transplants (PIT)
- 5 Pts had 1 PIT / 52 Pts had 2 PIT / 11 Pts had 3 PIT to achieve insulin independence
- At 5 years 80% had C-peptide present
- At 5 years 10% were insulin independent
- Mean duration of independence was 15 months
Complications

- Hepatic bleeding
- Hepatic infarct
- Splenic hemorrhage
- Portal HTN
- Portal vein thrombosis

- No hard stats on complications

Efficient use of organs

- Most patients need a total islet cell mass that must be prepared from two or more donors to become insulin independent
- Tissue availability will be the limiting factor
- Approx. 6000/yr cadaveric donors in US
- Est. that < ½ are suitable for Pancreas/Islet cell transplant (do the math)
Conclusion

- Until the logistic and islet cell yield (mass) problems have been solved, pancreas transplantation will remain the most efficient use of most donor organs.

- Pancreas transplant can be done at most transplant centers – however, Islet cell isolation requires a specialized facility – this lack of infrastructure makes it impossible to do on a large scale currently.
Conclusion

- Prospective and adequately powered clinical trials comparing islet cell transplant, pancreas transplant and intensive insulin therapy need to be obtained to determine a risk-to-benefit ratio.
- Islet cell transplant is still in its infancy and, thus, should only be performed in a controlled setting where facilities for performing this procedure are available.
- Pancreas transplant is now the---------------------- ------ established procedure for the successful surgical treatment of T1DM.