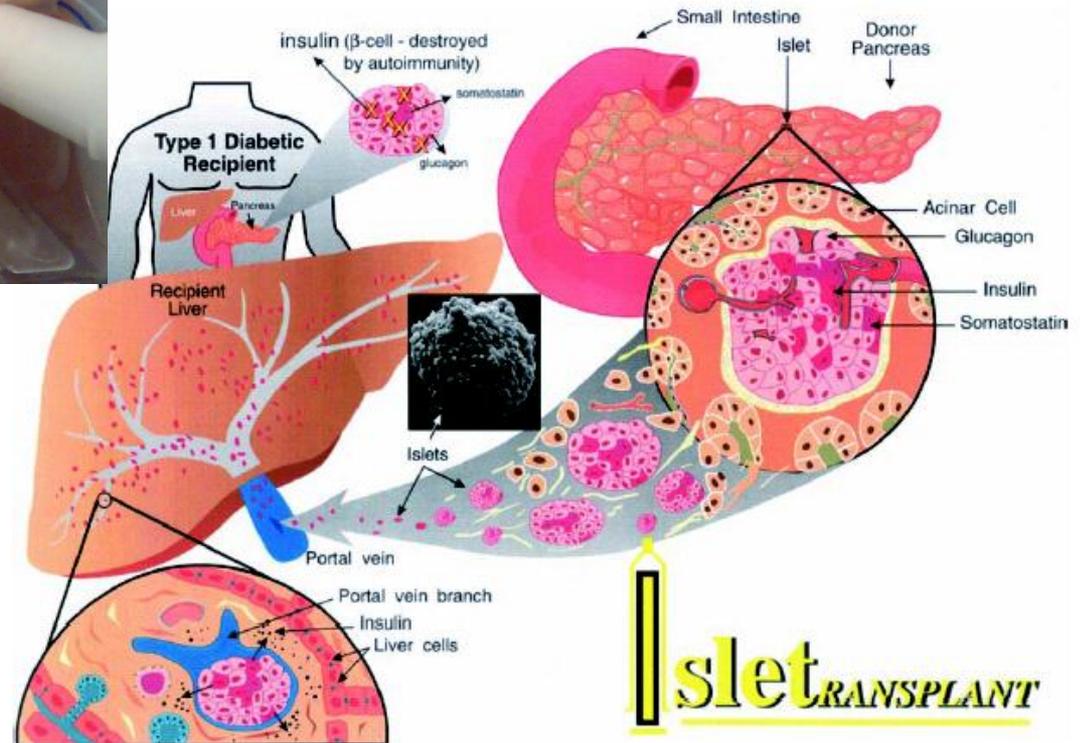
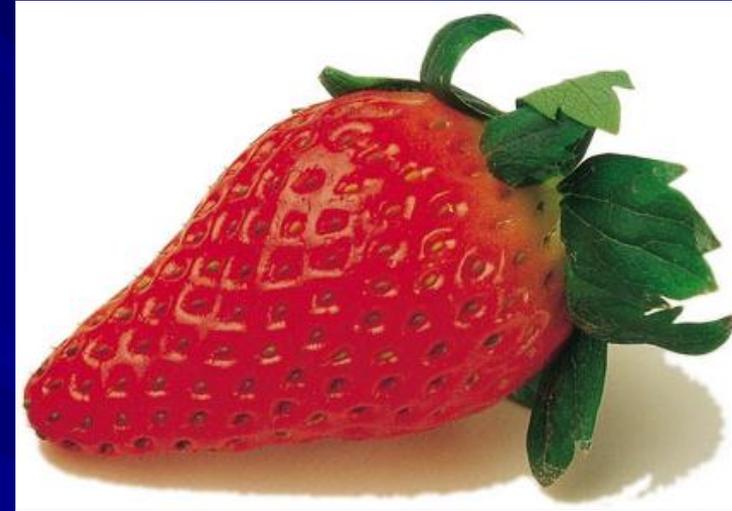


Simultaneous Pancreas-Kidney and Islets Transplantation



Diabetes Mellitus

Diabetes and its complications are the growing problem in nowadays world especially in developed countries



Kazi A, Blonde L.: Classification of diabetes mellitus.: Clin Lab Med 21:1, 2001

LaPorte RE, Matsushima M, Chang YF.: Prevalence and incidence of insulin-dependent diabetes In : National Diabetes Data Group. Diabetes in America 2nd ed. Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Disease 1995:37

Diabetes complications

Patients with insulin-dependend DM:

- ◆ **5 x blindness**
- ◆ **17 x kidneys failure**
- ◆ **5 x atherosclerosis**
- ◆ **2 x circulatory complications**
- ◆ **Life-time expectancy shorter by 30% then in healthy population**



Dr Alexis Carrel

Noble prize, 1912

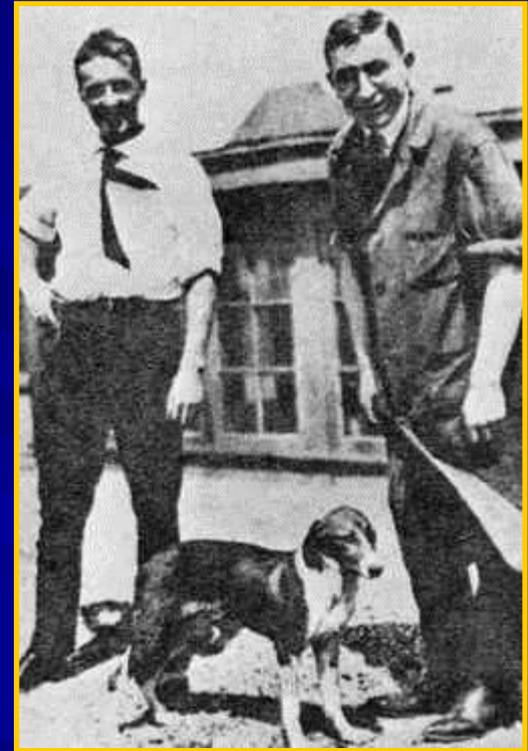
Insulin



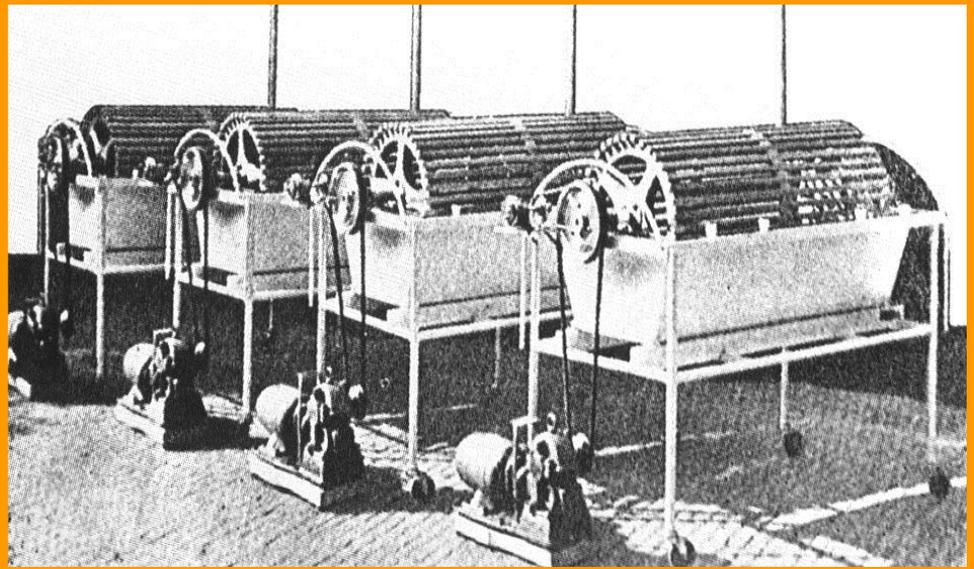
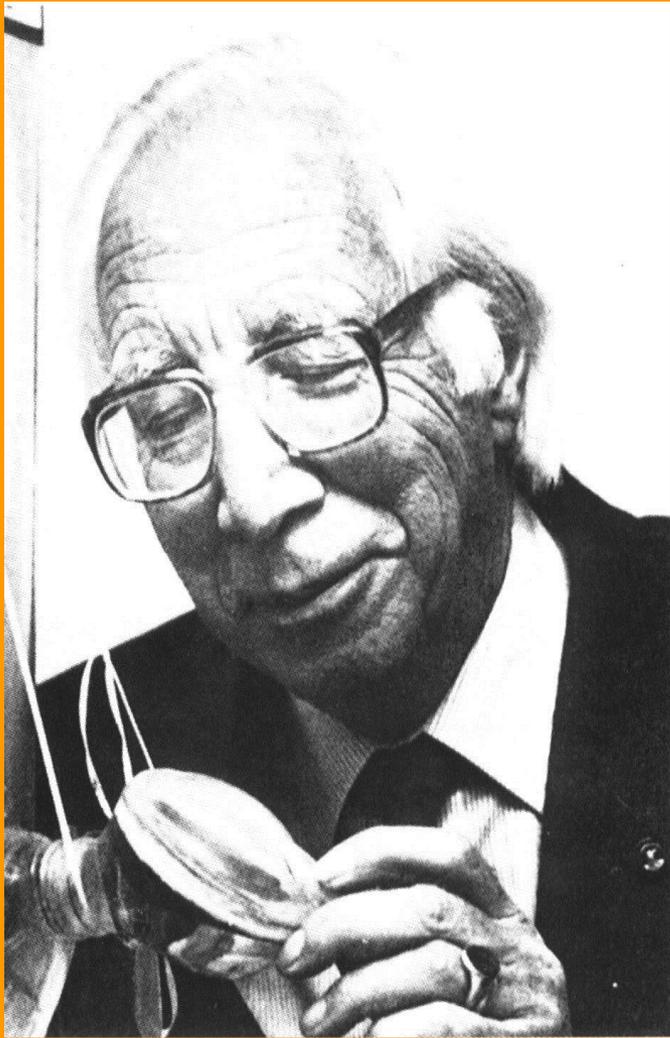
The internal secretion of pancreas.

Banting FG, Best C.:

J Lab Clin Med 1922, 7:256



Charles Best (left), Sir Frederick Banting (right) and Toto (middle)



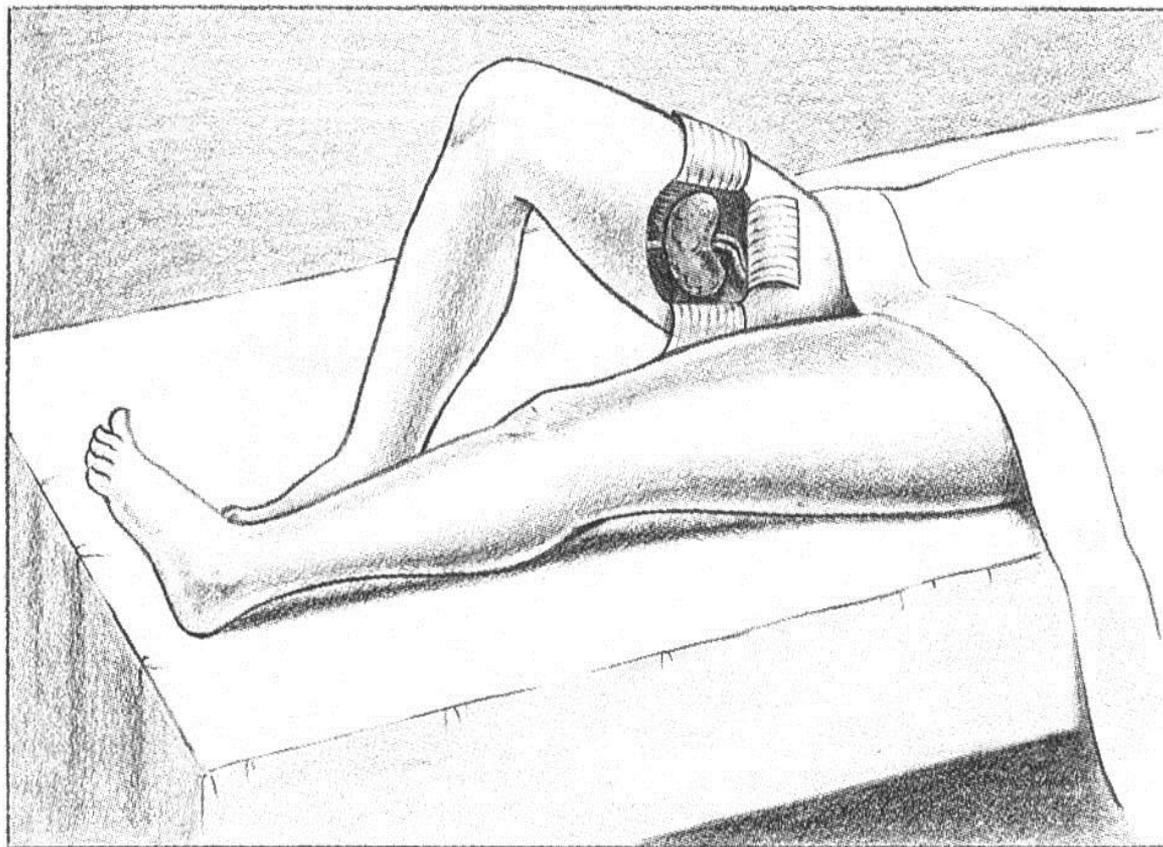
Kolff, 1945

**20% of patients with chronic renal failure are due to DM.
First cause of Renal failure in the developed countries.**



Voronov, 1933

ВРАЧЕБНОЕ ДЕЛО. № 9, 1950 г.





**First successful kidney
transplantation**

Boston, 1954

**Joseph Murray
John Merrill**

First successful Pancreas Transplantation

17 XII 1966

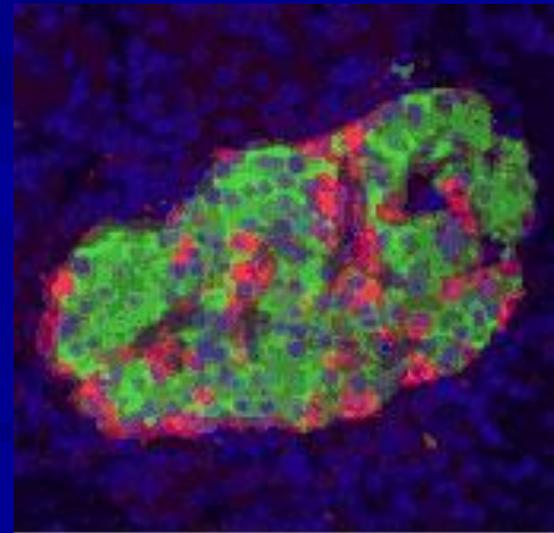
**W.D.KELLY, R.C. LILLEHEI
UNIVERSITY OF MINNESOTA**

History

Moskalewski S.

ISOLATION AND CULTURE OF THE ISLETS OF LANGERHANS OF THE GUINEA PIG.

Gen Comp Endocrinol. 1965 Jun;44:342-53.



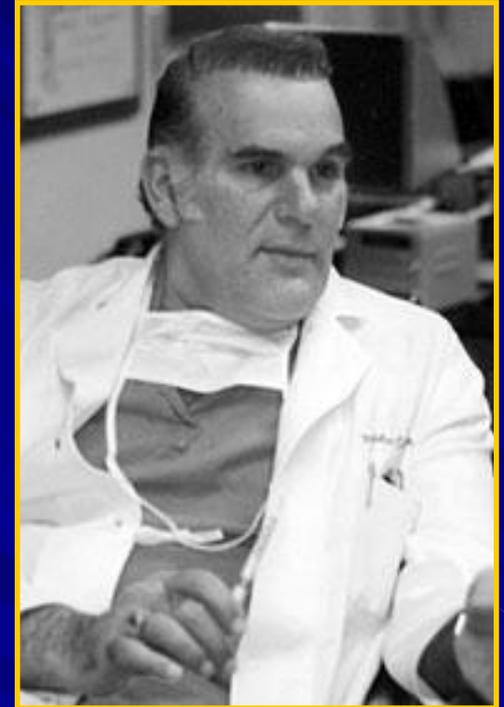
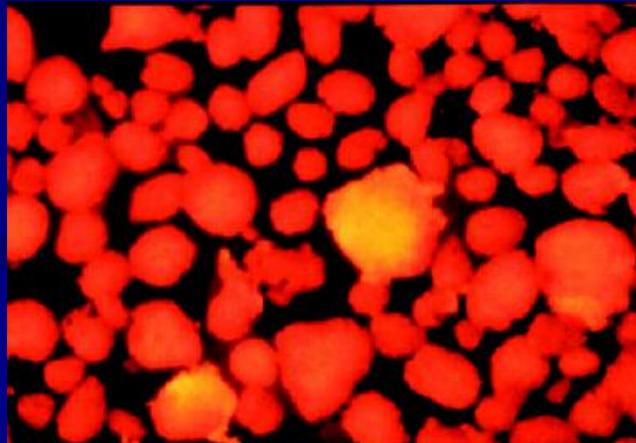
History



David Sutherland

1974 – First Islets
allotransplantation

1977 – first islet
transplantation from
living donor



John Najarian

1987 – unsuccessful pancreas
transplantation in Szczecin, prof. S
Zieliński

February 1988 – First successful Pancreas
Transplantation in Poland,

PROF. J. SZMIDT

CSK Banacha Warszawa

April 1988,

PROF. W. ROWIŃSKI, PROF. J.

WAŁASZEWSKI, PSK Nr 1 Warszawa ul.

Nowogrodzka 59

Islets allotransplantation

12 June 2008

In the Department of General and Transplantation Surgery

Piotr Fiedor, Michał Wszola, Andrzej Berman, Artur Kwiatkowski, Krystian Pawelec, Maciej Juszcak, Marek Paśnicki, Monika Krajewska, Dominika Dęborska, Adam Wernikowski, Łukasz Górski, Nina Wilewska, Magdalena Durlik, Janusz Wyzgał, Andrzej Chmura.



Do Surgeons fight for the pancreas whether to do whole organ transplantation or islets?

1. Brak ogólnych przeciwwskazań do pobrania narządów (zakażenia wirusowe, uogólnione zakażenie bakteryjne i grzybicze, nowotwór)
2. Wiek dawcy < 65 roku (preferowany poniżej 50 roku)
3. Brak wywiadu dotyczącego cukrzycy typu I i II
4. Brak w wywiadzie ostrego zapalenia trzustki
5. Brak w wywiadzie alkoholizmu i narkomanii
6. Bez zatrucia tlenkiem węgla, metanolem
7. Bez urazu trzustki
8. Donors BMI >24; Donors weight not less then 50 kg
9. Ciśnienie skurczowe ↑ 100 mmHg
10. Amylaza we krwi < 100 U/L

Donor for the Pancreas Tx

Donor for the Islets Tx

Transplantation • Volume 76, Number 3, August 16, 2004

Procurement of the Human Pancreas for Pancreatic Islet Transplantation

Timothy C. Lee,¹ Neal R. Barshes,¹ F. Charles Brunicaudi,¹ Rodolfo Alejandro,² Camillo Ricordi,² Liz Nguyen,¹ and John A. Goss^{1,3}

Table 1. Applying Accepted Criteria in Practice

Criterion	Number of donors
Age 15–40 years	20
ICU stay < 7 days	19
No clinical signs of infection	20
Negative viral tests	20
No hypotension	17
No cardiac arrest	16
Serum amylase < 300	19
Hyperglycemia < 300	18
No history of pancreatic disease	20
No history of abdominal trauma	20
No history of alcohol addiction	20
BMI < 25	17
Correct kidney function	19
Time of pancreatic ischemia < 12 hours	19



Transplantation Proceedings, 35, 2337–2338 (2003)

Simultaneous Pancreas-Kidney Transplantation: Analysis of Donor Factors

G. Michalak, A. Kwiatkowski, J. Czenwiński, A. Chmura, W. Lisik, M. Kosieradzki, M. Wszola, S. Fesołowicz, M. Bieniasz, J. Wałaszewski, and W. Rowiński

Pancreas allocation in the world

Annals of Surgery • Volume 240, Number 4, October 2004

Transplantation for Type 1 Diabetes

Comparison of Vascularized Whole-Organ Pancreas With Isolated Pancreatic Islets

Adam Frank, MD, Shaoping Deng, MD, Xiaolan Huang, MD, Ergun Velidedeoglu, MD, Yong-Suk Bae, BS, Chengyang Liu, MD, Peter Abt, MD, Robert Stephenson, MD, Muhammad Mohiuddin, MD, Thav Thambipillai, MD, Eileen Markmann, RN, Maral Palanjian, RN, Marty Sellers, MD, Ali Najj MD, PhD, Clyde F. Barker, MD, and James F. Markmann MD, PhD

... we believe that pancreas transplantation and islet transplantation should continue to coexist as complimentary methods.



Transplantation Proceedings, 35, 1625–1627 (2003)

Current Status of Beta-Cell Replacement Therapy (Pancreas and Islet Transplantation) for Treatment of Diabetes Mellitus

D.E.R. Sutherland

tion can be life saving.^{26,27} Pancreas transplantation, and eventually islet transplantation, should be in the armamentarium of every transplantation center for the treatment of patients with diabetes.

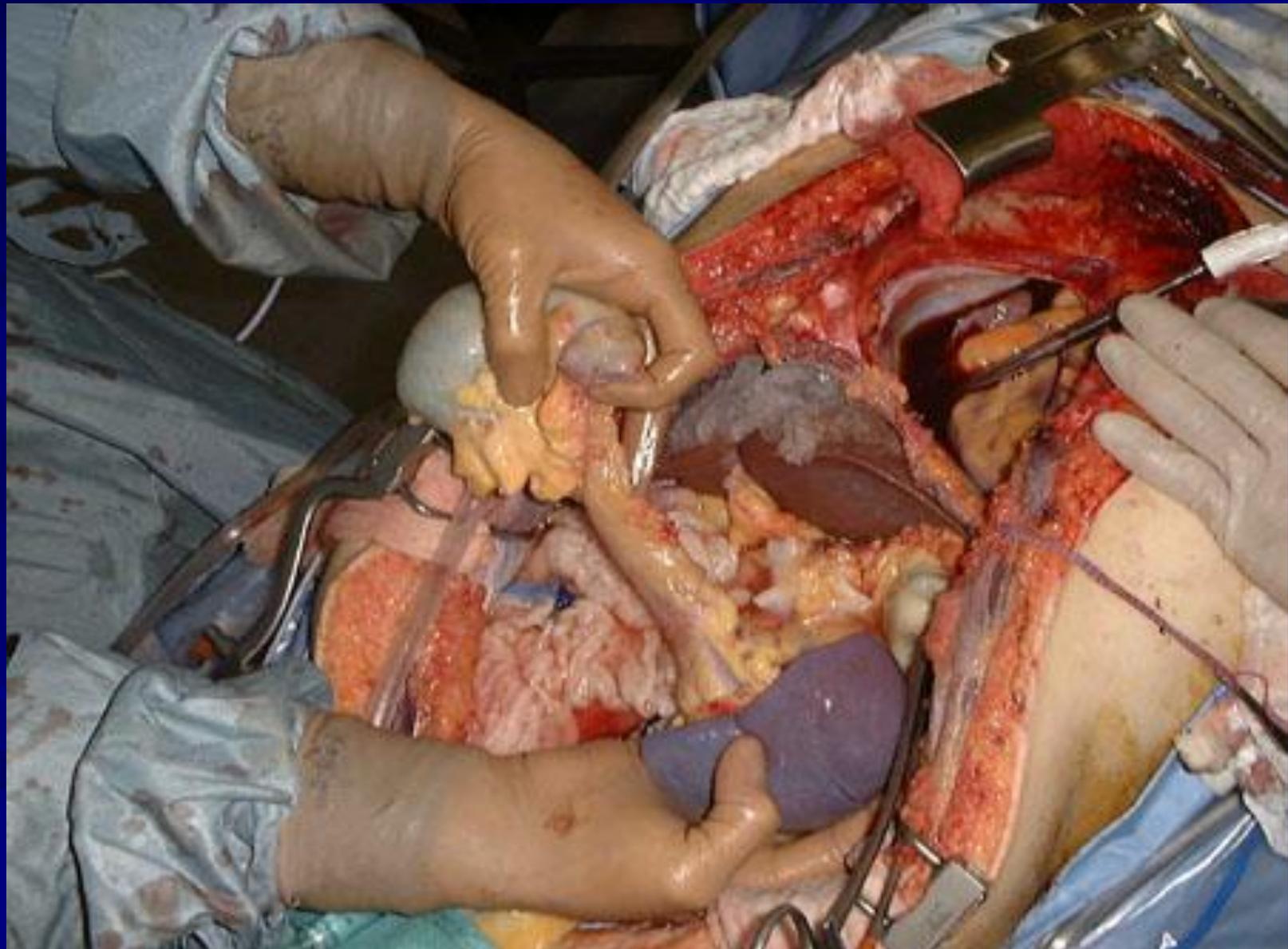
American Journal of Transplantation 2004: 4 763 – 766.

Are Criteria for Islet and Pancreas Donors Sufficiently Different to Minimize Competition?

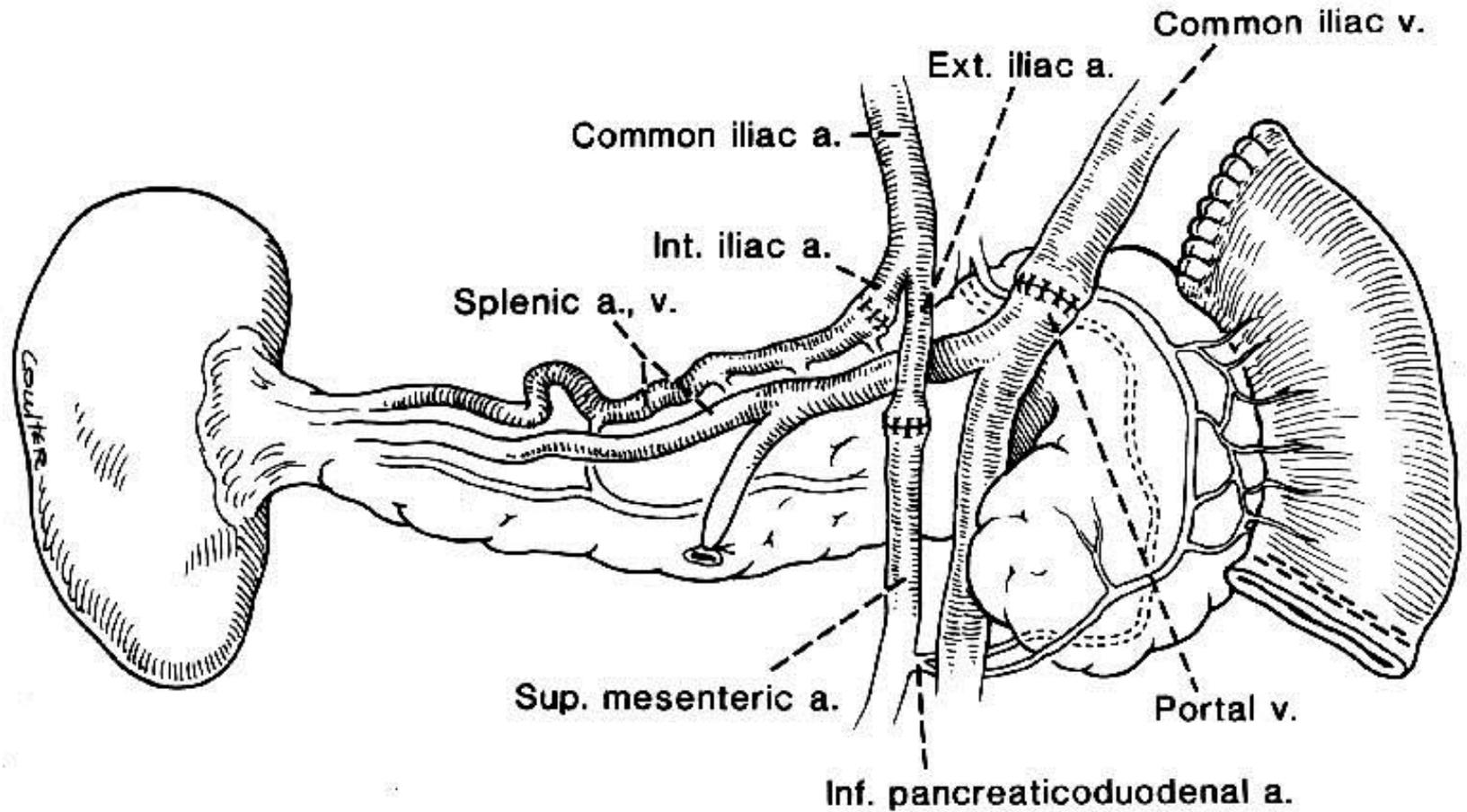
Fredric Ris, Christiano Toso, Florence Unno Veith, Pietro Majno, Philippe Morel and Jose Oberholzer

In our analysis we gave priority to pancreas transplantation (...)Our analysis indicates that in the mean time, using the specified selection criteria, allocations for islets can be made from a sufficient number of donors for the field to progress even while allowing all cadaveric donors organs meeting both pancreas and islet criteria to be used for pancreas transplants.

Pancreas retrieval



Vessels reconstruction



Pancreas transplantation

Recipients

SPKTx

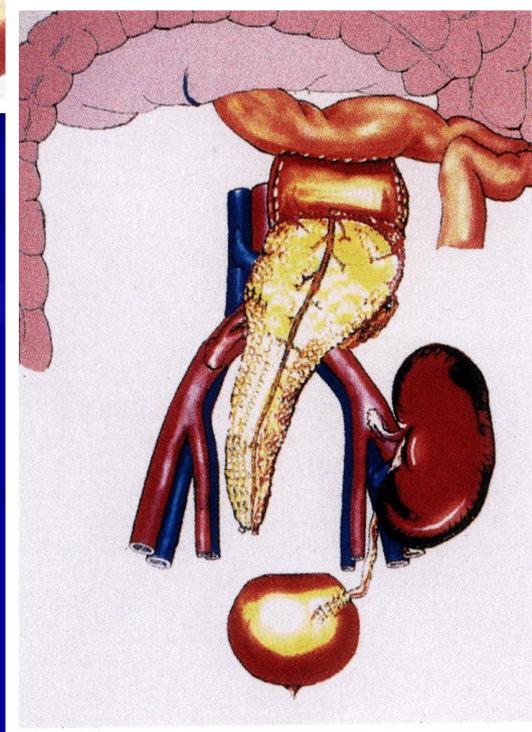
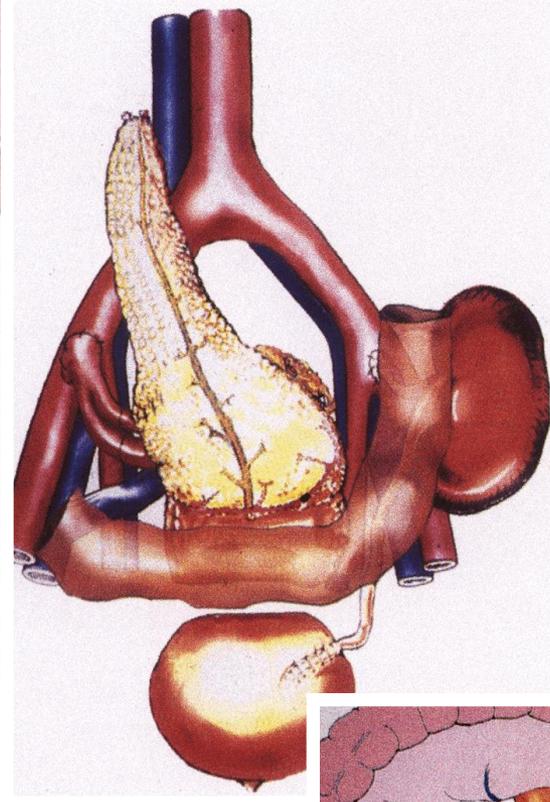
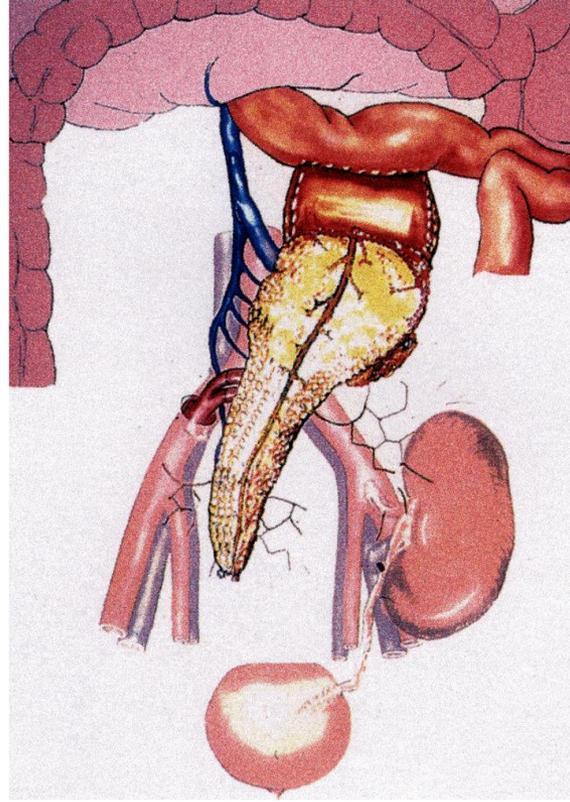
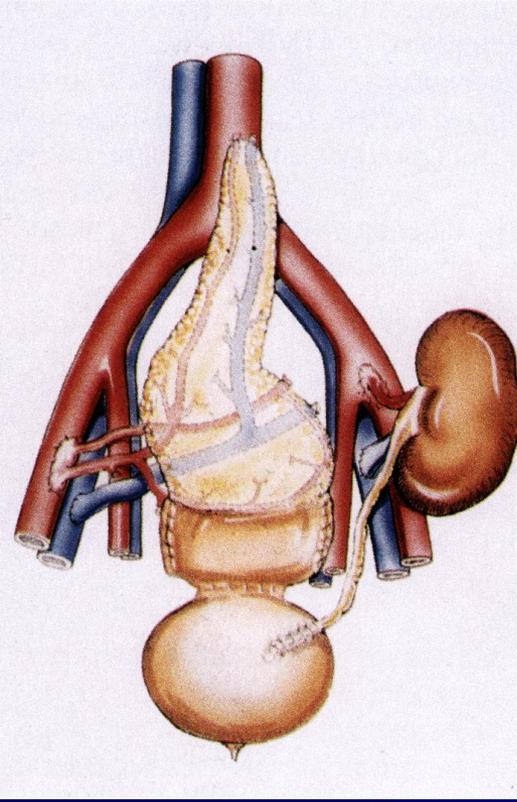
Diabetic kidneys' nephropathy

PTA

Diabetic complications without renal failure

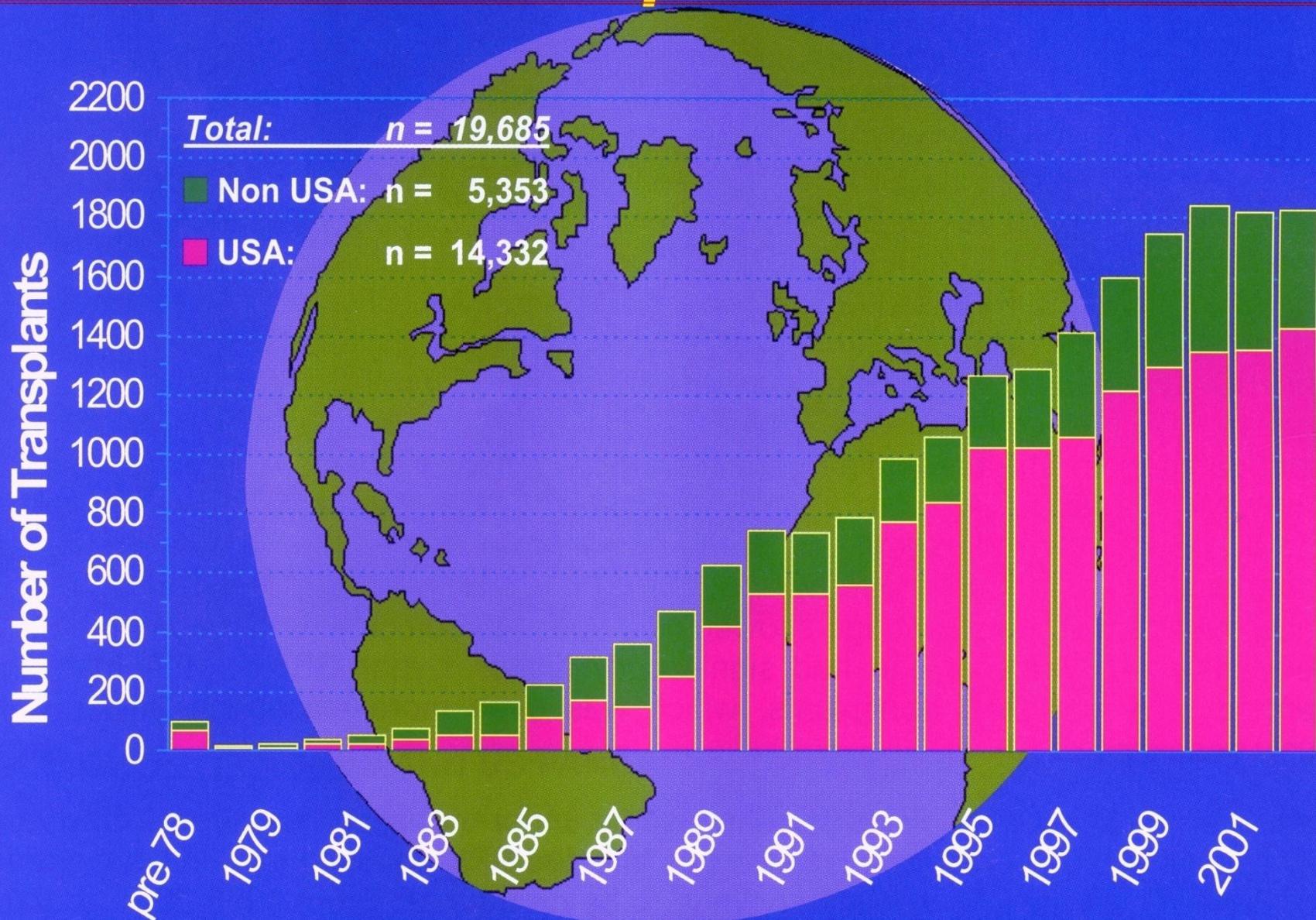
PAK

Unsuccessful SPKTx or pancreas discharged from retrieval during harvesting of kidney



Types of SPKTx

Pancreas Transplants Worldwide



IMMUNOSUPPRESSION

◆ Four – drugs therapy

- Antibodies
- PROGRAF
- MMF
- Steroids



Surgical complications (52%)

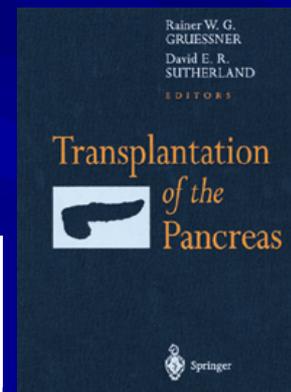
- Vessels thrombosis
- bleeding
- Fistula
- Intraabdominal abscesses
- Pancreas abscesses
- Pancreatitis

Islets transplantation

Type I DM

(negative peptide C)

1. Duration of illness > 5 years
2. Metabolic instability (>2 hypoglycemia episodes or >2 hospitalizations due to ketoacidosis within last year)
3. Hypoglycemia unawareness
4. Developing diabetic complications: proliferative retinopathy, albuminuria > 300 mg/dl, neuropathy



Transplantation of the pancreas.
Gruessner RWG, Sutherland DER.
Springer 2003

Pancreas and Islet transplantation.
Hakim N, Stratta R, Gray D.
Oxford University Press 2002



JAMA[®]

The Journal of the American Medical Association

JAMA, February 16, 2005—Vol 293, No. 7

Single-Donor, Marginal-Dose Islet Transplantation in Patients With Type 1 Diabetes

Bernhard J. Hering, MD
Raja Kandaswamy, MD
Jeffrey D. Ansite, BS
Peter M. Eckman, MD
Masahiko Nakano, MD, PhD
Toshiya Sawada, MD
Ipppei Matsumoto, MD, PhD
Sung-Hee Ihm, MD
Hui-Jian Zhang, MD
Jamen Parkey, PA-C, MPH
David W. Hunter, MD
David E. R. Sutherland, MD, PhD

Islets after Kidney Tx



Transplantation Proceedings, 36, 603–604 (2004)

Islet Transplantation in Type 1 Diabetic Patients

F. Bertuzzi, A. Secchi, and V. Di Carlo

Type I DM after KTx

(negative peptide C)

1. Age < 65 years
2. > 6 after KTx
3. Creatinine < 2mg/dl
4. Creatinine clearance > 60 ml/min
5. Proteinuria < 300 mg/day



Transplantation Proceedings, 36, 1121–1122 (2004)

Islet of Langerhans Allogeneic Transplantation at the University of Geneva in the Steroid Free Era in Islet After Kidney and Simultaneous Islet-Kidney Transplantations

T. Berney, P. Bucher, Z. Mathe, A. Andres, D. Bosco, R. Mage, C. Toso, J. Oberholzer, C. Becker, J. Philippe, L. Bühler, and P. Morel

ISLET TRANSPLANTATION is a promising procedure for treatment of type I diabetic patients. The main indications for islet transplantation are: (1) type I diabetic patients already under immunosuppressive therapy for other transplantations (kidney, liver); (2) patients with

Excluding criteria

1. BMI > 26 kg/m² (K) lub > 27 (M)
2. Weight > 75 kg
3. Daily insulin intake > 0,7U/kg mc or > 50 U/day
4. Chronic liver failure/portalhypertension

Islets Tx



Transhepatic approach



Transplantation of islets of Langerhans:
new developments

*T. Berney^{a,b}, L. Bübler^{a,c}, A. Caulfield^b, J. Oberholzer^a, Ch. Toso^a, R. Alejandro^b, D. K. C. Cooper^c,
C. Ricordi^b, Ph. Morel^b*

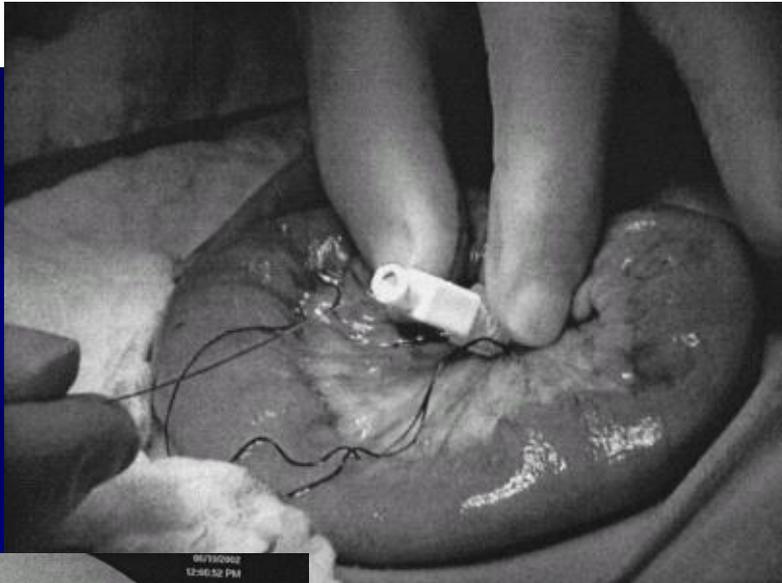
SWISS MED WKLY 2002;132:671-680

Islets Tx

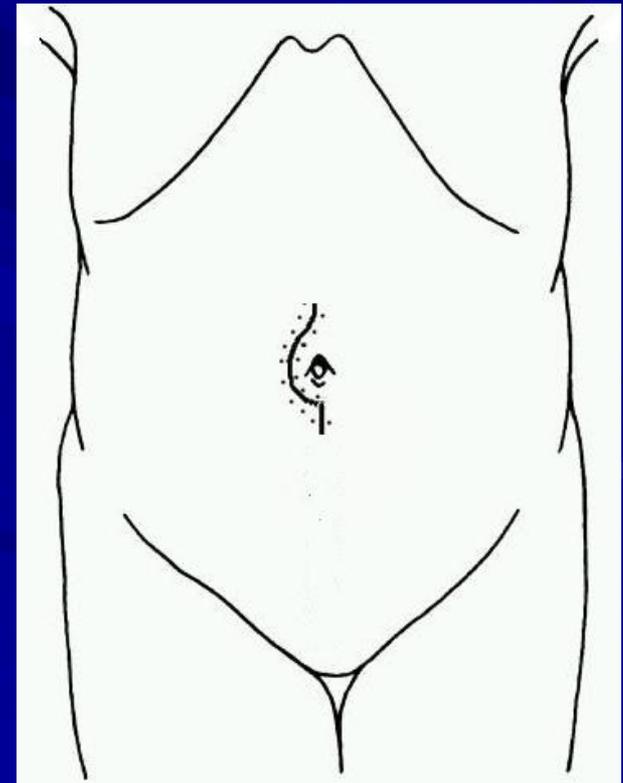
INSULIN INDEPENDENCE ACHIEVED USING THE TRANSMESENTERIC APPROACH TO THE PORTAL VEIN FOR ISLET TRANSPLANTATION

A. OSAMA GABER,^{1,4} ABBAS CHAMSUDDIN,² DANIEL FRAGA,¹ JONATHAN FISHER,¹ AND AGNES LO³

TRANSPLANTATION Vol. 77, No. 2 January 27, 2004



Laparotomy

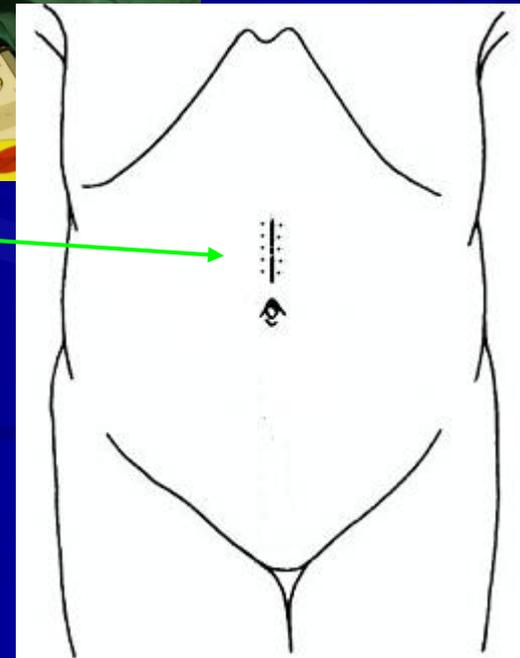


Small incision

Our allotransplantation



Islets Tx



Insulin intake

U



HbA1c

Before ITx – 7,2%

After ITx (90 days)- 5,9%

Immunosuppression



Transplantation Proceedings, 39, 179–182 (2007)

Second Annual Analysis of the Collaborative Islet Transplant Registry

N. Close, R. Alejandro, B. Hering, and M. Appel for the CITR Investigators

Protocol from Edmonton (NEJM, Jul 27, 2000; 230-9.)

- ✓ 10 – tygodniowy leczenie **daclizumabem** – 1 mg/kg mc co 14 dni
- ✓ **Tacrolimus** – 1 mg/ dziennie następnie do uzyskania stężenia w surowicy 6-10 ng/ml
- ✓ **Sirolimus** – dawka początkowa - 0,2 mg/kg mc następnie 0,1 mg/kg mc – stężenie w surowicy – 12 – 15 ng/ml

Modified protocol from Edmonton (AJT, 2002;2: 674-677.)

- ✓ 10 – tygodniowy leczenie **daclizumabem** – 1 mg/kg mc co 14 dni (lub **simulect**)
- ✓ **Tacrolimus** – 1 mg/ dziennie następnie do uzyskania stężenia w surowicy 6-10 ng/ml
- ✓ **Prednisolone** – 500 mg, 250 mg, 125 mg
- ✓ **MMF** – 3g/dzień następnie konwersja **Sirolimus** – dawka początkowa - 0,1 mg/kg mc – stężenie w surowicy – 6 – 12 ng/ml

Table 3. Immunosuppression Regimen at Time of First Infusion

	Overall	
	N	%
Total	118	100.0
Sirolimus + tacrolimus + daclizumab	73	61.9
Sirolimus + tacrolimus + daclizumab + infliximab	12	10.2
Sirolimus + tacrolimus + basiliximab + etanercept	5	4.2
Sirolimus + tacrolimus + MMF + methylprednisolone + anti-thymocyte globulin + daclizumab + infliximab + etanercept	5	4.2
Sirolimus + tacrolimus + 15-deoxyspergualin + daclizumab	5	4.2
Sirolimus + tacrolimus + hOKT3γ-1(Ala-Ala)	3	2.5
Sirolimus + tacrolimus + MMF + daclizumab	2	1.7
Sirolimus + tacrolimus + MMF + methylprednisolone + anti-thymocyte globulin + daclizumab + etanercept	2	1.7
Neoral cyclosporine + methylprednisolone + everolimus + anti-thymocyte globulin + infliximab + etanercept	2	1.7
Sirolimus + MMF + anti-thymocyte globulin + daclizumab	1	0.8
Neoral cyclosporine + methylprednisolone + anti-thymocyte globulin + etanercept	1	0.8
Missing information on immunosuppression	7	5.9

World results

International Islet Transplant Activity (1999-2004)

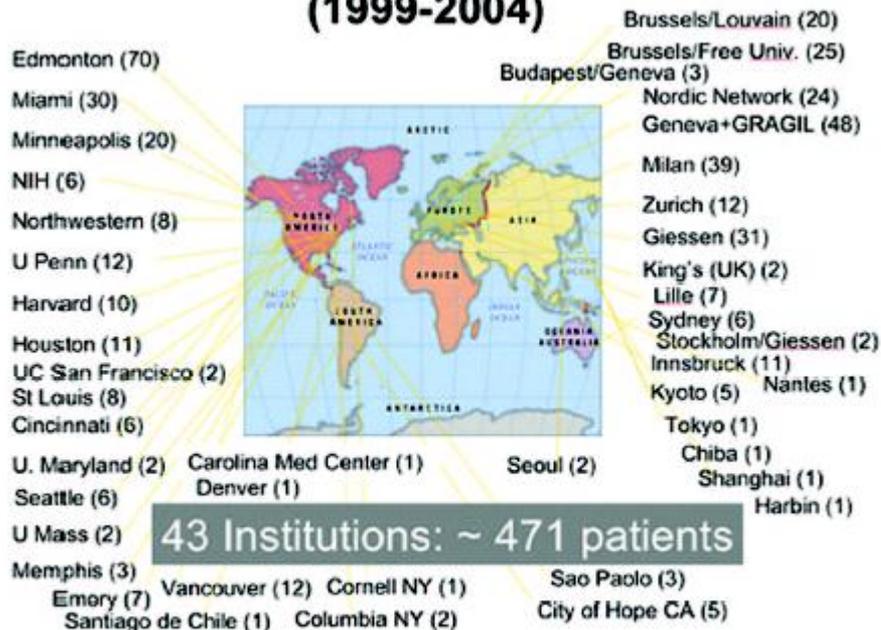
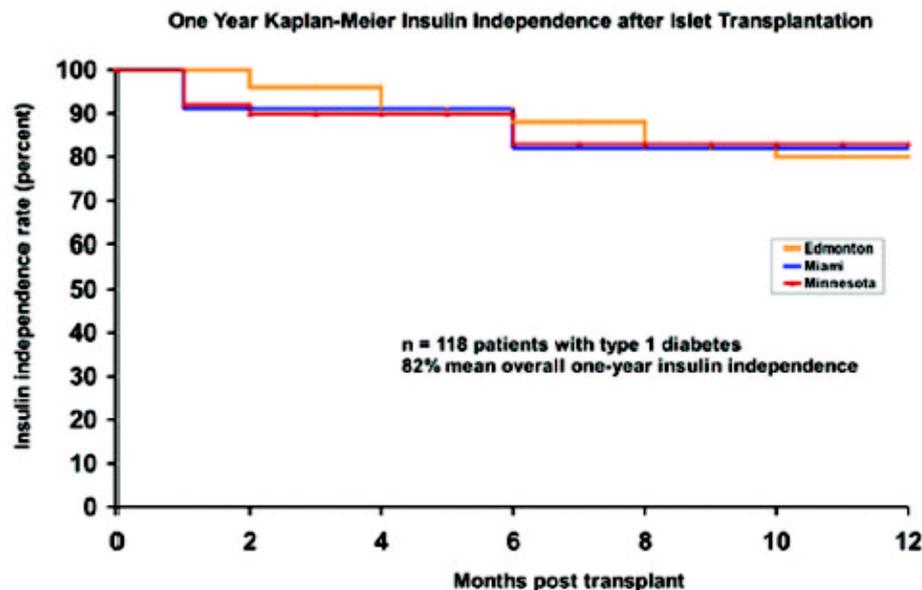


FIGURE 1. Exponential increase in clinical islet transplant activity within the most recent five years, with patients transplanted at 43 international institutions.



World results

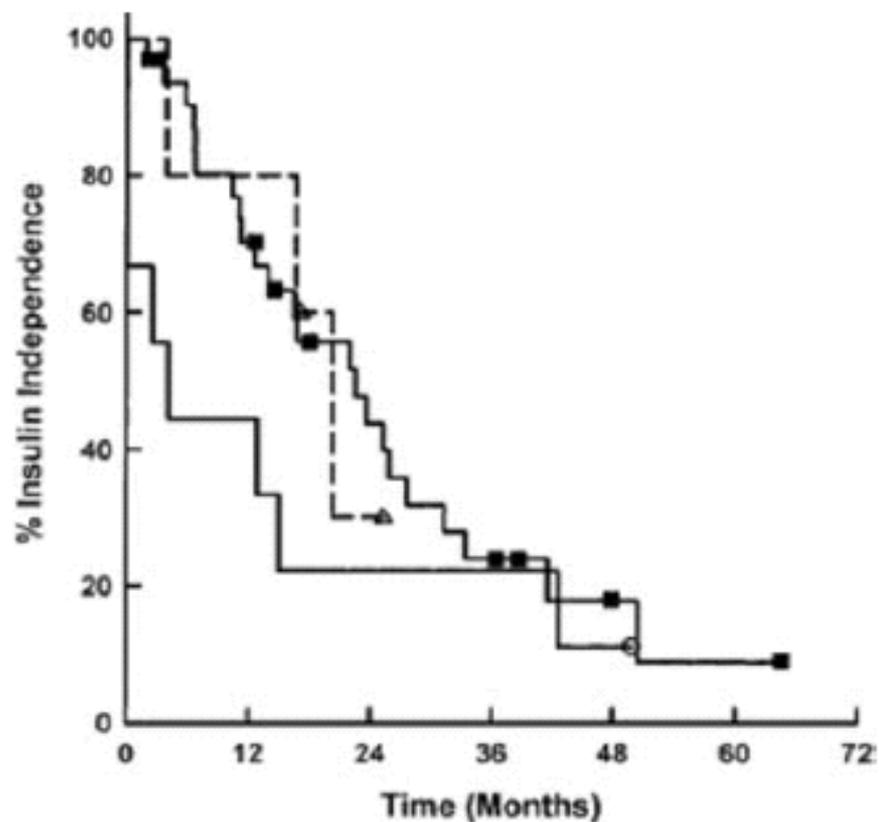


Figure 1: Survival analysis for insulin independence over time for all those who completed the islet transplant procedures depending on whether they required only one (---△---) (n = 5 initially and n = 3 for final timepoint), two (---■---) (n = 33 initially and n = 3 for final timepoint), or three (---●---) (n = 9 initially and n = 4 for final timepoint) transplant procedures. Copyright © 2005 American Diabetes Association from Diabetes, Vol. 54, 2005; 2060–2069. Reprinted with permission from the American Diabetes Association.

Thank You for Your attention
michal.wszola@wp.pl

