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Transplantation of Isolated Pancreatic Islets into the Portal Vein of Diabetic Rats

RECENT work from this laboratory indicates that intraperitoneal transplantation of isolated pancreatic islets ameliorates the effects of experimental diabetes in rats[1]. Although the intraperitoneal siting of these islets reduces the hyperglycaemia and polyuria of streptozotocin induced diabetes in these animals, consistently normal values for blood sugar and urine volume are rarely achieved.

In normal circumstances, insulin from the pancreatic β-cells is secreted directly into the portal venous system and we have investigated the possibility that this intraportal site may provide a more physiological environment for the transplanted islets and possibly more effective use of secreted insulin.

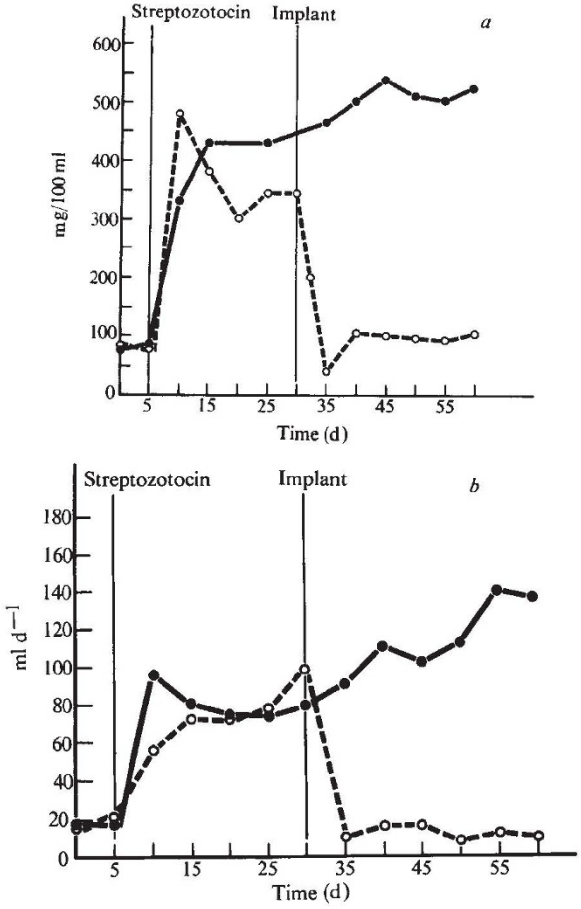

Fig. 1 Effect of portal vein implantation of pancreatic islets on the blood glucose (*a*) and urine (*b*) volumes of diabetic rats. (Mean of ten diabetic controls and five portal vein implants.) Values after transplantation: diabetic controls (●) blood sugar 270 to 720 mg%; urine volumes 80 to 150 ml daily; portal vein implant (○) blood glucose 66 to 140 mg%; urine volume 6 to 20 ml daily.

Pancreatic islets were collected from Lewis rats by the collagenase digestion method of Lacy and Kostianovsky[2] and separated from unwanted acinar debris by differential layering of dialysed 'Ficoll'[3]. This technique involves the mixing of digested pancreas with 'Ficoll' 25% (w/v) and the careful layering above this mixture of 'Ficoll' in decreasing concentrations (23%, 20% and 11%). Centrifugation for 10 min at 800*g* leaves the acinar tissue in the 25% 'Ficoll' while islets rise through the density gradient to settle at the 20–11% interface. The isolated islets (400–600) were then injected through a 1 ml siliconized syringe and No. 23 needle into the portal vein of diabetic Lewis rats of the same inbred strain as the donors. Diabetes had been induced in these recipient rats 3 weeks before by the intravenous injection of streptozotocin (65 mg kg^{-1}) and the study included a group of ten diabetic rats as control animals.

After the transplantation operation all rats were returned to their metabolic cages and observed for 4 weeks during which a free diet of rat chow and water was allowed. Urine volumes were measured daily and blood glucose levels estimated on alternate days.

The ten control animals were grossly diabetic with blood glucose levels varying between 270 and 720 mg/100 ml and urine volumes between 80 and 150 ml daily. Direct injection of pancreatic islets into the portal vein resulted in normoglycaemia and normal urine volumes in the five rats studied (Fig. 1).

These results suggest that if transplantation of isolated pancreatic islets is to be used in the treatment of clinical diabetes the portal venous system may be the site of choice for maximal effectiveness.

CHARLES B. KEMP
MICHAEL J. KNIGHT
DAVID W. SCHARP
PAUL E. LACY
WALTER F. BALLINGER

Departments of Surgery and Pathology,
Washington University School of Medicine,
St Louis, Missouri

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Sulphate Conjugation and L-Dopa Treatment of Parkinsonian Patients

CONJUGATION of catecholamines in man was first described for adrenaline by Richter in 1940[1]. He suggested that the conjugated product was an ester of sulphuric acid. Richter and MacIntosh[2] later demonstrated that conjugation of adrenaline markedly reduced its pressor properties and proposed that conjugation is a mechanism of inactivation of the biological properties of this amine. Holtz and Credner[3] administered L-dopa to several animals including man and isolated both free and conjugated dopamine (DA) from urine. Conjugation of two metabolites of DA, homovanillic acid (HVA) and 3,4-dihydroxyphenylacetic acid (DOPAC), was observed by Shaw, McMillan and Armstrong[4] when they isolated these two phenolic acids from the urine of human subjects who had received L-dopa orally. The conjugates of these compounds can be isolated by anion exchange chromatography[5,6]. When conjugated derivatives in the eluates from anion exchange columns were hydrolysed by sulphuric acid[5,6] or sulphatase[5], the unconjugated parent compounds were identified by paper chromatography.