

Letters to the Editor

LIVER TRANSPLANTATION FROM LIVE DONORS

SIR,—A liver transplant programme in Brazil began in September, 1985, but by November, 1988, only 15 adults and 4 children had been transplanted due to shortage of cadaveric organ donors, a problem faced in many other countries. By the end of the 3rd year of our programme the probability that a potential recipient would die while on the waiting list was 50% for adults and 73% for children.

A technique for liver transplantation from live donors has been developed at our laboratory. Hepatic segments II and III (left lateral) are resected and transplanted to the recipient, whose liver has already been removed with preservation of the entire inferior vena cava. The graft is placed in the hepatic fossa in an obverse position, which favours perfect alignment of the vascular stumps. The risk of haemorrhage in the donor is reduced by a simple device, described elsewhere.¹

Patient 1

On Dec 8, 1988, we did our first human liver transplant from a living donor. The recipient was a 4½-year-old girl in terminal advanced liver failure due to biliary atresia. Her 23-year-old mother, a healthy ABO-identical woman, was the donor. The operation took 18 h. The donor did not need any blood or blood derivatives and was discharged on the 4th postoperative day. The child recovered well at first and the graft started to produce bile soon after the operation. Severe haemolysis resulted from haemolytic antibodies inadvertently transfused in two bags of plasma, with ensuing anuric renal failure. The child died 6 days after the operation during haemodialysis to control metabolic disturbances and fluid overload.

Patient 2

On July 21, 1989, we operated on a 19-month-old girl, blood type A, with hepatic fibrosis and Caroli's disease. No donor suitable on vascular criteria could be found among her relatives studied by angiography. A 40-year-old, blood type O healthy man volunteered for organ donation. The operation lasted 16 h. The donor was discharged on the 5th day, and again no blood or blood products were used. The recipient was alert soon after the operation, being extubated on the 1st day. The graft showed signs of preservation injury, manifest by delayed production of bile. Coagulation and biochemical indices of hepatic function improved until the 4th post-transplant day, when a severe episode of acute cellular rejection was noticed. This event was controlled by OKT-3 monoclonal antibody (Ortho, Raritan, New Jersey). By Aug 16 (26th post-transplant day) the patient was showing clinical, laboratory, and histological evidence of full recovery from the rejection episode. She is alert and is being orally fed. Liver enzymes have dropped to nearly normal levels. She is still jaundiced, with a serum total bilirubin of 30 mg/dl but she began to produce bile again on day 24.

We have also been following up the donors. The first donor made an uneventful recovery and became pregnant 2 months after her operation. Donor 2 is also in good general condition. He had a febrile episode around the 10th postoperative day but there was no evidence of an abdominal complication and he responded to antibiotic therapy. He is already back at work.

Liver transplantation from a live donor may be life-saving in children with terminal liver disease for whom a cadaveric donor is not available.

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HLA-DQ β NON-ASP-57 ALLELE AND INCIDENCE OF DIABETES IN CHINA AND THE USA

SIR,—Children in the United States are about twenty times more likely to acquire insulin-dependent diabetes mellitus (IDDM) than children in China, incidence rates for white children in Allegheny County, Pennsylvania,¹ and for children in Tianjin² being 15.8 and 0.7 per 100 000 per year, respectively. This huge variation in incidence is unexpected but may be due, in part, to genetic differences across populations and specifically associated with the polymorphism in position 57 of the HLA-DQ β chain.

Genetic susceptibility (or resistance) to IDDM in whites is strongly related to variation in a short segment of the HLA-DQ β chain gene.^{3,4} The presence of at least one allele leading to aspartic acid in position 57 (Asp-57 or *A*) of this chain seems to protect against IDDM, while a non-charged amino acid in the same position (non-Asp-57 or *NA*) is associated with increased susceptibility. Among probands in the IDDM registries in Allegheny County, 96% were *NA/NA*, 4% were heterozygous, and none was *A/A* (table). *NA* homozygosity was significantly associated with IDDM, with an estimated relative risk of 107.³

The contribution of the non-Asp-57 genetic marker to IDDM in non-US populations has not been well studied. To see if variations in the prevalence of this DNA polymorphism could explain the different incidence of IDDM in Allegheny County and Tianjin we examined the association between *NA* and IDDM in the Chinese. DNA amplified by the polymerase chain reaction from 18 Chinese IDDM patients and 25 unrelated healthy Chinese controls was tested with nine DQ β allele-specific oligonucleotide probes. Of the 18 patients only 1 was *NA/NA*, and 13 were heterozygous, while among the 25 Chinese controls, 23 were *A/A* (table).

If *A* is protective in both populations the allele distributions observed in diabetic patients should directly reflect the proportions of genetically susceptible individuals. Thus, one would expect to find a higher prevalence of *NA/NA* among whites with IDDM than among the Chinese diabetic patients, who would more likely be heterozygous. The large proportion of *A/A* homozygous individuals in the Chinese controls is consistent with the low incidence of IDDM in China. The association between *NA* and IDDM should be strong in both populations.

Although we cannot directly evaluate the relative risk for *NA* homozygosity among the Chinese because no control was *NA/NA*, an indirect approach was possible. On an assumption of Hardy-Weinberg equilibrium we calculated gene frequencies in the general Chinese population for *A* ($q^2=0.92$, $q=0.96$) and for *NA* ($p=1-0.96=0.04$), giving a prevalence of *NA/NA* homozygosity of 0.0016 or about 1 in 600 among non-diabetic Chinese. These estimates yield a relative risk (and 95% confidence interval) associated with *NA* homozygosity among the Chinese of 35 (0.8-1502), which, though lower, was not significantly different from that observed for US whites of 107 (14, 368) since the confidence intervals overlap. Despite the small numbers, the relative risk associated with *NA* homozygosity is high, and potentially similar, in both populations.

The high prevalence of *NA/A* heterozygosity among the Chinese IDDM patients suggests a "dose response" in terms of disease susceptibility. 11 of the 13 heterozygous Chinese patients were positive for the DQw 3.1 (an Asp-57 allele), which has been considered "neutral" in terms of its diabetogenic effect.⁴ This provides further evidence that the "protection" conferred by DQw 3.1 might not be as strong as that of other Asp-57 alleles. Such an effect may be operative in other populations; and if sufficient IDDM cases were evaluated, individuals heterozygous and/or

HLA-DQ PHENOTYPES IN US AND CHINESE IDDM CASES AND CONTROLS

HLA-DQ	US whites		Chinese	
	Diabetics (n=27)	Non-diabetics (n=123)	Diabetics (n=18)	Non-diabetics (n=25)
<i>NA/NA</i>	26 (96%)	24 (19.5%)	1 (6%)	0
<i>NA/A</i>	1 (4%)	57 (46.3%)	13 (72%)	2 (8%)
<i>A/A</i>	0	42 (34.1%)	4 (22%)	23 (92%)