

become useful as a provocative and predictive test for early renal abnormalities.

In summary, our data indicate that exercise microalbuminuria is not detected in most kidney donors and support the notion that the uninephrectomized state does not result in a progressive hyperfiltration nephropathy. In addition, longitudinal studies could reveal whether a particular subset of donors with abnormal exercise albuminuria represent an early phase of overt proteinuria and kidney damage.

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CYCLOSPORINE AND ITS METABOLITES IN MOTHER AND BABY

Cyclosporine (CsA) is a potent immunosuppressive agent that has significantly improved allograft survival in recipients of human organ transplants (1, 2). Recently there have been a few cases of successful pregnancies in transplant patients receiving CsA alone or in combination with steroids (3, 4). A general concern regarding pregnancy in transplant patients is the potential harmful effect of chronic maternal immunosuppression on the fetus. It is essential to determine the extent of exposure of the fetus to the immunosuppressive drug and its metabolites. We recently studied the concentrations of CsA and several of its metabolites in maternal and cord blood, placenta, and the umbilical cord in two patients receiving chronic CsA therapy.

The first patient was a 26-year-old woman with primary biliary cirrhosis secondary to common bile duct obstruction who received a successful liver transplantation in November 1985. Immunosuppression was achieved with CsA and steroids. During the second postoperative week she also received the monoclonal antibody OKT 3. In February 1987, she delivered a 3208 g baby boy. At the time of delivery she was receiving CsA 200 mg orally b.i.d., prednisone 10 mg, hydralazine 50 mg q.i.d., ferrous sulphate 300 t.i.d, furosemide 40 mg q.d. and multivitamin therapy. On the day of the delivery she received CsA at 10 A.M. and the baby was born at 5:45 P.M. Maternal blood was obtained at 8.5 hr after CsA administration while cord blood was obtained at 7.8 hr after CsA administration. Maternal and cord blood along with placenta and umbilical cord were analyzed for CsA and several of its metabolites using

a gradient high-pressure liquid chromatographic method developed in our laboratory (5).

The second patient was a 25-year-old woman who received an orthotopic liver transplant in November 1985 for cirrhosis of unknown cause. Immunosuppression was achieved with CsA and steroids. Four weeks following the transplant, the patient developed cytomegalovirus hepatitis from which she recovered with reduction in immunosuppression. She did well for 10 months and then developed biliary obstruction that was corrected surgically. At this time she became pregnant. Pregnancy was complicated by anemia requiring blood transfusions and preeclampsia. At gestational age 36 weeks, she had a caesarean section because of fetal distress, and a live baby boy (weight 1690 g) was delivered at 8 A.M. At the time of delivery her medications included Riopan 30 ml p.o. every 4 hr, ranitidine 150 mg orally b.i.d., ferrous sulfate 300 mg orally t.i.d., prednisone 15 mg orally every day and CsA 125 mg orally every 12 hr. Maternal and fetal cord blood were drawn simultaneously at the time of delivery 10 hr after the previous oral cyclosporine dose. The baby had intrauterine growth retardation, as the weight and head circumference were below the fifth percentile. The blood samples, umbilical cord, and placenta were refrigerated at 4°C until analyzed by HPLC.

Table 1 lists the concentrations of CsA and its metabolites in blood and in different tissues. The highest concentration of CsA was seen in the umbilical cord of patient 1. The placenta contained CsA concentrations nearly five to ten times greater than the maternal and the fetal blood, and had the highest

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TABLE 1. Cyclosporine and its metabolites in mother and child^a

	Maternal blood (ng/ml)	Cord blood (ng/ml)	Placenta (ng/g)	Umbilical cord (ng/g)
Cy A	90, 105	53, 55	506, 318	2641, <25
M-17	134, 132	159, 162	481, 184	137, 97
M-21	<25, 0	0, 0	<25, 0	0, 0
M-1	89, 63	28, 0	229, 89	28, 0
M-18	0, <25	0, 0	0, 0	0, 0

^a The first value was observed in patient 1 and the second value was observed in patient 2.

concentrations of all the metabolites measured. While small concentrations of M 21 were observed in the placenta and the maternal blood of patient 1, M 18 concentrations were below measurable levels in most of the specimens.

Cyclosporine is very lipid-soluble, extensively distributed in the body, and highly metabolized. Previous studies have reported the presence of CsA in cord blood, placenta, amniotic fluid, and breast milk (4). In addition to CsA, we have observed high concentrations of CsA metabolites in the placenta, indicating the presence of CsA metabolizing enzymes in this tissue and/or accumulation of these metabolites in the placenta. Very high concentrations of CsA (nearly 30 times that of the maternal blood) were also observed in the umbilical cord of one patient. Some of the metabolites, particularly M 17, appear in very high concentrations in the blood and also possess significant immunosuppressive effect (6, 7). Whether the metabolites of CsA also contribute to the toxicity is not known. In this study we report for the first time the concentrations of CsA metabolites in cord blood, placenta, and umbilical cord. Of interest is the relatively high concentration of all the metabolites in the placenta.

While no specific harmful effects attributable to CsA were observed in the baby, it is clear that the fetus is exposed not only to CsA but also to its metabolites. According to the tests conducted by Sandoz Inc. (Basel, Switzerland) CsA is not mutagenic in the Ames test and did not produce any chromo-

somal abnormalities in animals. However, since the fetus is exposed to chronic CsA and its metabolites, the immediate septic complications and the possible long-term effects on gestationally immunosuppressed children should be investigated.

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MYCOTIC ANEURYSM OF THE HEPATIC ARTERY COMPLICATING HUMAN LIVER TRANSPLANTATION

Reconstruction of the hepatic artery is an essential step in human hepatic transplantation. Thrombosis of the hepatic arterial anastomosis posttransplantation is the most frequent arterial complication (1, 2), particularly in small children (3). Mycotic aneurysms involving the hepatic arterial anastomosis are reported to occur much less frequently. In a series of 86 orthotopic hepatic transplantations performed (46 in children at the Cochin Hospital we have observed three cases of hepatic artery thrombosis. We have had two cases of anastomotic mycotic hepatic artery aneurysms occurring in the early post-operative period. The aim of this article is to discuss the diagnostic circumstances and therapeutic options of this serious complication, and to analyse the consequences of the resection of the aneurysm with deliberate ligation of the hepatic artery, which was the treatment used in our two patients.

Case 1. An 18-year-old female patient suffering from cirrhosis due to chronic active viral hepatitis (type B) was transferred to the Cochin Hospital on 8/18/86 for hepatic transplantation. She had previously undergone an elective distal splenorenal

shunt for bleeding esophageal varices, following which hepatic function had continued to deteriorate. Clinically, she was deeply jaundiced with significant wasting. Prothrombin index was 22%. On 9/11/86, an orthotopic hepatic transplantation without extracorporeal venovenous bypass was performed using the liver of a 19-year-old man. No antibiotic was administered to the donor. Cold ischemia time was 5 hr 20 min and the anhepatic phase was 1 hr 20 min. The hepatic arterial anastomosis between the recipient hepatic artery proper and the donor common hepatic artery was performed with continuous 7/0 prolene. Biliary continuity was reestablished with a Roux-en-Y hepaticojejunostomy. The splenorenal anastomosis was permeable and was not suppressed. Intraoperative transfusion was 25 units of packed cells. Routine immunosuppression with corticosteroids and cyclosporine was commenced. Mezlocillin, gentamycin and ornidazole were administered during the first 48 hr. On the 12th postoperative day the patient became febrile and suffered an intraabdominal hemorrhage. A CT scan showed a subhepatic hematoma, and angiography showed a small he-