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## Letters to the Editor

## LIVER TRANSPLANTATION FOR WILSON'S DISEASE

SIR,-We have reported before on the early course two patients after liver transplantation for Wilso disease.1.2 The indication for operation in the first recipient was liver failure. This boy, who is now aged 17 years, will be six years post-transplantation on July 15. He is the longest survivor in the world after liver replacement. With the provision of a new liver, a decoppering process was demonstrated, mainly by a prolonged cupriuresis. However, the potential usefulness of the metabolic observations in the context of Wilson's disease and its treatment was reduced by certain atypical features of the case. Although the copper concentration in the native liver was very high, the serum cæruloplasnin concentration was low normal and the corneas had evidence of Kayser-Fleischer rings.

The second patient is now four years two mones post-transplantation.

He was first diagnosed as having Wilson's disease at the age of 11 years. By the age of 14 years, he had progressively deteriorating

## BIOCHEMICAL FINDINGS BEFORE AND AFTER TRANSPLANTATION

_	Normal values	Relation to operation			
		Preop.	3 mo. postop.	17 mo. postop.	42 mo. postop.
Liver-copper (µg./g.)	< 20	184	_	45	27
Serum-copper (µg./100 ml.)	70-118	22-4-35	149	74	73
Ceruloplasmin (mg./100 ml.)	22-49	1.0-1.7	74	48	32
Urine copper (µg./24 hr.) s.g.o.r. (I.U./l.)	< 30 3-27	540 25	119 70	80 25	87 15
Serum-bilirubin (mg./100 ml.)	< 1.0	2.9	0-4	0-64	0.5

hepatic and neurological function. Although he had ascites, transplantation was recommended more because of the serious neurological impairment than because of liver failure. He hid crippling dystonia, dysarthria, and choreoathetosis. There were prominent Kayser-Fleischer rings. Liver-function tests inclu d a serum-bilirubin of 2.9 mg. per 100 ml., a prothrombin-tim of 44%, and serum protein and albumin concentrations of 5.7 and 2.9 g. per 100 ml., respectively. He showed no response to D-penicillamine and triethyltetramine dihydrochloride.

On March 23, 1971, orthotopic hepatic transplantation was carried out. Postoperatively, immunosuppression included cyclophosphamide (for which azathioprine was later substituted), prednisone, and a three-month course of heterologous antilymphocyte globulin. Presently, his liver function is normal (see accompanying table).

As previously reported, his liver removed at transplantation had a markedly increased copper content (see table). Biopsies of the homograft at twelve, thirteen, and seventeen months arter transplant showed tissue-copper levels of 48, 30, and 45 µg. per g. wet weight, respectively. In the most recent biopsy at forty- wo months, the tissue-copper level was 27 µg. per g. wet weight only slightly above normal (see table). All the homog aft biopsies appeared normal histologically.

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Urinary copper excretion was 540 µg, per 24 hours before operation. In the early postoperative period this patient had markedly increased urinary excretion of copper, but after five months a decrease toward normal was noted. At the present hime, the urinary copper excretion is 87 µg. per day, which is will slightly elevated.

Initially, ceruloplasmin was virtually absent in the serum of this patient, but within three months after transplantation it increased dramatically and now remains normal (see table). The terum-copper concentration, which was low preoperatively, pepidly increased early postoperatively, then fell to normal.

Postoperatively, the patient's neurological dysfunction has radually improved and now he has no neurological impairment. he Kayser-Fleischer rings have completely disappeared over a period of two and a half years as determined by several slit-lamp

The complete correction, in our second patient, of all the classical clinical manifestations and biochemical bnormalities of Wilson's disease has not been reported with other forms of therapy. These observations lend import to the contention that this genetic disorder is ever-based. With the provision of a normal liver, excess sody-copper is eliminated over a period of years.

This work was supported by research grants from the Veterans dministration; by grants Al-AM-08898 and AM-07772 of the Regional Institutes of Health; and by grants RR-00051 and R-0069 from the General Clinical Research Centers Program the Division of Research Resources, National Institutes of akh.

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ROBERT W. BEART, JR. CHARLES W. PUTNAM K. A. PORTER THOMAS E. STARZL.

## SULPHONE RESISTANCE IN LEPROSY

Sir,—The salutary paper by Dr Pearson and his fileagues (July 12, p. 69) confirms a growing suspicion that sulphone-resistant leprosy bacilli may be shown to be pearing with disturbing frequency wherever the instigation of clinical relapse can be supplemented by ouse footpad inoculation. Several instances are known have arisen in England, in addition to the one reported Adams and Waters.

The financial and other constraints which, in most funtries, have hitherto made monotherapy in leprosy adings reported. For patients with lepromatous leprosy, testment with more than one leprostatic drug should aceforth be the ideal to strive for, if not actually andatory.

While Dr Pearson and his colleagues state that "the duration of treatment before relapse is very striking' d cite one patient who relapsed after only 5 years of termittent treatment, it should be known that, in a gerian patient, relapse due to dapsone-resistant organisms curred after 52 months of regular treatment at a dose of ing. twice weekly.

Fortunately, no case of relapse due to sulphone-resistant Tenisms has so far failed to respond to clofazimine.

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S. G. BROWNE.

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