Letters to the Editor

LIVER TRANSPLANTATION FOR WILSON'S DISEASE

SIR,—We have reported before on the early course of two patients after liver transplantation for Wilson's 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 cæruloplasmin concentration was low normal and the corneas had no evidence of Kayser-Fleischer rings.

The second patient is now four years two months 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 hepatic and neurological function. Although he had ascites, transplantation was recommended more because of the serious neurological impairment than because of liver failure. He had crippling dystonia, dysarthria, and choreoathetosis. There were prominent Kayser-Fleischer rings. Liver-function tests included a serum-bilirubin of 2·9 mg. per 100 ml., a prothrombin-time 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.

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
Cæruloplasmin (mg./100 ml.)	22–49	1·0–1·7	74	48	32
Urine copper (μg./24 hr.) ..	< 30	540	119	80	87
s.g.o.t. (i.u./l.)	3–27	25	70	25	15
Serum-bilirubin (mg./100 ml.)	< 1·0	2·9	0·4	0·64	0·5

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

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 time, the urinary copper excretion is 87 μg. per day, which is still slightly elevated.

Initially, cæruloplasmin 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 serum-copper concentration, which was low preoperatively, rapidly increased early postoperatively, then fell to normal.

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

The complete correction, in our second patient, of all the classical clinical manifestations and biochemical abnormalities of Wilson's disease has not been reported with other forms of therapy.[3] These observations lend support to the contention that this genetic disorder is liver-based. With the provision of a normal liver, excess body-copper is eliminated over a period of years.

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SULPHONE RESISTANCE IN LEPROSY

SIR,—The salutary paper by Dr Pearson and his colleagues (July 12, p. 69) confirms a growing suspicion that sulphone-resistant leprosy bacilli may be shown to be appearing with disturbing frequency wherever the investigation of clinical relapse can be supplemented by mouse footpad inoculation. Several instances are known to have arisen in England, in addition to the one reported by Adams and Waters.[4]

The financial and other constraints which, in most countries, have hitherto made monotherapy in leprosy almost obligatory, must now be reviewed in the light of the findings reported. For patients with lepromatous leprosy, treatment with more than one leprostatic drug should henceforth be the ideal to strive for, if not actually mandatory.

While Dr Pearson and his colleagues state that "the long duration of treatment before relapse is very striking", and cite one patient who relapsed after only 5 years of intermittent treatment, it should be known that, in a Nigerian patient, relapse due to dapsone-resistant organisms occurred after 52 months of regular treatment at a dose of 100 mg. twice weekly.[5]

Fortunately, no case of relapse due to sulphone-resistant organisms has so far failed to respond to clofazimine.[6]

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