outcome was good but relapses were frequent and the long term outcome was disappointing. All were mentally retarded, only 4% were seizure free at follow-up and 42% had behavioral problems. When examined at 2½ to 19 years of age, 58% had partial or focal, often secondary generalized seizures, and 37% had myoclonic astatic or Lennox-Gastaut syndrome. The dose of ACTH was 20-40 IU daily for six weeks in eight children and 80-140 IU daily in 14 children. Arterial hypertension occurred in ten, two developed cardiac failure, three had fluid retention in the cysts of polycystic kidneys and developed hypertensive crises during therapy. Infections (otitis, gastroenteritis, pneumonia) occurred in four. (Riikonen R, Simell O. Tuberous sclerosis and infantile spasms. Dev Med Child Neurol March 1990; 32:203-209).

COMMENT. The demonstration of cerebral calcifications by CT in all patients with tuberous sclerosis at an early age is of interest. The necessity for abdominal ultrasound in diagnosis and before ACTH therapy is indicated by the study. The dosage of ACTH used was exceptionally large and would have accounted for the unusually high incidence of side effects and frequency of arterial hypertension. Many authorities are content with much smaller doses, 10 and at the most 20 IU of ACTH daily given for shorter periods (three weeks) and repeated at intervals when necessary. Early treatment with ACTH is important in terms of the response of infantile spasms to therapy and possibly in relation to subsequent development (Gordon N. Dev Med Child Neurol April 1990, 32:363). In the present study of patients with tuberous sclerosis and infantile spasms, early treatment with large doses of ACTH provided an initial good response but the long-term outcome was poor despite prolonged administration.

CARBAMAZEPINE TOXICITY

Three children who developed acute liver failure while taking carbmazepine are reported from the Department of Child Health, King's College Hospital, Denmark Hill, London, England. A girl aged 11 developed a severe maculopapular rash, intermittent fever, arthralgia, anemia, and vomiting four weeks after starting carbamazepine. The blood concentration was 32 mcmol/l (therapeutic range 16-50). She developed jaundice two weeks later and on admission six days later she had a generalized exfoliative rash, periorbital edema, generalized lymphadenopathy, and hepatomegaly. Her platelets and differential white count were normal. Concentrations of IgG, IgM, and IgE were increased. Liver biopsy showed acute hepatitis. Steroid treatment with prednisolone (0.7 mg/kg/24 hours) caused a dramatic symptomatic and biochemical improvement. She was discharged one week later after complete recovery and prednisolone was stopped after 18 days. The second child, aged 7, again presented with fever, generalized maculopapular rash, arthralgia, and lymphadenopathy four weeks after starting carbamazepine. She developed jaundice, ascites, and generalized edema 17 days later. Total bilirubin concentration was 236 mcmol/l. Hepatic encephalopathy developed four days after admission and the child died of infectious complications three months after a liver transplantation. The third patient, a 3 year old child,

had a fulminant hepatic failure due to carbamazepine toxicity which was treated successfully by transplantation. (Hadzic N et al. Acute liver failure induced by carbamazepine. Arch Dis Child March 1990; 65:315-317).

COMMENT. The authors identified three previous cases of fatal acute liver failure directly attributable to carbamazepine, one in a child. Four other children with fatal hepatitis while on carbamazepine were also taking several drugs, some being potentially hepatotoxic such as phenytoin. Clinical and laboratory findings in the authors cases suggested an immunoallergic reaction although only one patient improved with steroids. It was suggested that determination of liver function during the first few weeks of treatment and early detection of signs of idiosyncrasy may help detect patients at risk of developing acute liver failure. Two of the three patients had rash preceding the development of jaundice. A warning to the parents to discontinue medication at the first sign of skin rash might be more important than reliance only on serial liver function tests. Two cases of carbamazepine-induced liver failure were reported at the 1989 meeting of the Child Neurology Society (Murphy JV et al). At the recent 42nd annual meeting of the AAN there were two reports of systemic lupus erythromatosis induced by carbamazepine and the manufacturer (Ciba-Geigy) had knowledge of 18 unpublished cases. (Neurology April 1990; 40:Suppl I:137).

VALPROATE TOXICITY

Facial and limb edema in seven patients during long-term valproate therapy are reported from the Montefiore/Einstein Epilepsy Center, Albert Einstein College of Medicine, Bronx, NY. Ages ranged from 6 to 43 years; four were 6 to 17 years. All received dosages greater than 1500 mg/day for a prolonged time and trough levels ranged from 36 to 107 mcg/ml. Four patients were receiving other medications. All had normal liver and renal function tests. Reduction in the edema occurred in four following a reduction in valproate dosage, and one resolved spontaneously. (Ettinger A, Moshe S, Shinnar S. Edema associated with long-term valproate therapy. Epilepsia March/April 1990; 31:211-213).

COMMENT. In a recent case report of a three year old boy from Japan a fulminant hepatic failure induced by valproate was associated with a marked increase in W-oxidation of the drug. The patient died on the seventh hospital day and autopsy findings showed acute liver necrosis with congestion and cholestasis. (Kuhara T et al. Epilepsia March/April 1990; 31:214-217). Valproate-induced thrombocytopenia was reported in a total of 35 patients at the 42nd annual meeting of the AAN. (Delgado et al: Sherbany AA et al. Neurology April 1990; 40 (Suppl I):136-137). Close monitoring of platelet counts is recommended particularly when high doses of valproate are necessary in treatment of children with epilepsy. Thrombocytopenia may develop after several years of therapy and seems to be dose related.