affected. The changes differed clearly from those in glycogenosis II where glycogen storage is membrane bound and is found in most skin cells including fibroblasts, sweat glands, smooth muscle fibers, endothelial cells, and Schwann cells. Skin biopsy appeared to be useful in diagnosis of glycogenosis III and its differentiation from other glycogen storage disorders. (Sancho S et al. Skin biopsy findings in glycogenosis III: Clinical, biochemical, and electrophysiological correlations. Ann Neurol May 1990; 27:480-486).

COMMENT. Glycogen storage disease type III (debrancher deficiency, Cori-Forbes disease) is an autosomal recessively inherited disease with a deficiency in amyl-1,6-glycosidase or debrancher enzyme. Enzyme deficiencies occur in liver, muscle, heart, leukocytes, erythrocytes, fibroblasts, and muscle cultures. Abnormal glycogen storage is found in liver, muscle, and erythrocytes. Clinically there are three types, 1) infantile, 2) childhood, 3) adult type. The infantile type is associated with hypoglycemia, failure to thrive, and hepatomegaly. Symptoms usually remit partially with growth. Childhood types present with heart failure and exercise intolerance. Adults develop gradual weakness and wasting of distal muscles and may have a history of abdominal enlargement with hepatic dysfunction in early childhood. EMG shows diffuse myopathic changes. Growth failure and hepatic dysfunction including hypoglycemia have been improved by the administration of cornstarch (Borowitz SM, Greene HL. J Pediatr Gastroenterol Neutr 1987; 6:631).

TOXIC DISORDERS

FETAL HYDANTOIN SYNDROME

In a prospective study of 19 pregnancies monitored by amniocentesis at the Center for Human Genetics and the Meyer Rehabilitation Institute, University of Nebraska, Omaha, an adverse outcome was predicted for four fetuses on the basis of low epoxide hydrolase activity (30% of standard). The mothers were receiving phenytoin monotherapy and the infants had clinical characteristics of the fetal hydantoin syndrome. Fifteen fetuses with enzyme activity above 30% of the standard had no features of the syndrome. The authors suggest that this enzymatic biomarker may be useful in the prediction of infants at increased risk for congenital malformations induced by anticonvulsant drugs. (Buehler BA et al. Prenatal prediction of risk of the fetal hydantoin syndrome. N Engl J Med May 31, 1990; 322:1567-72).

COMMENT. Anticonvulsant drugs that are metabolized to form oxidative intermediates (epoxides) pose the greatest teratogenic risk to the fetus. The measurement of the enzyme involved with the biotransformation of the epoxide to a less toxic metabolite may serve as a biomarker of the fetus at high risk for the fetal hydantoin syndrome.

The clinical characteristics of the fetal hydantoin syndrome include upturned nose, midfacial hypoplasia, long upper lip, absent cupid's bow, hirsutism of face, back, arms, and legs, nail hypoplasia, hypotonia with delayed motor development, and poor weight gain.

PHENOBARBITAL-INDUCED DEPRESSION

Twenty-eight epileptic children aged six to 16 years were assessed for psychopathology in relation to anticonvulsant monotherapy at the Western Psychiatric Institute and Clinic, Children's Hospital of Pittsburgh and Mercy Hospital, Pittsburgh, PA. Eight patients were treated with phenobarbital, 17 carbamazepine, and three had been withdrawn from their anticonvulsant regimen. The phenobarbital treated group showed a higher rate of major depression than did those treated with carbamazepine or no anticonvulsant (38% vs 0%). The frequency of suicide attempts was similar between groups (13% vs 12%). The phenobarbital treated group had higher scores on the Children's Depression Inventory than did the carbamazepine treated patients. The patients who discontinued phenobarbital therapy recovered from major depressive disorder whereas those who continued the treatment remained depressed. (Brent DA et al. Phenobarbital treatment and major depressive disorder in children with epilepsy: A naturalistic follow-up. Pediatrics June 1990; 85:1086-1091).

COMMENT. Despite the relative safety of phenobarbital compared to other anticonvulsants, the increasing number of reports regarding adverse effects on behavior and cognition preclude its use in children whenever possible. Patients should be monitored closely for symptoms of an affective disorder and intellectual deterioration, and if signs of depression or regression are detected, a change to an alternative anticonvulsant should be considered. (See PNB January 1990; 4:2).

BENZODIAZEPINE-INDUCED CONGENITAL MALFORMATIONS

The potential teratogenic properties of benzodiazepine (BZD) intake during early pregnancy were investigated at the Departments of Pediatrics, Pathology and Genetics at Goteborg University, Sweden. Four neonatal diagnoses of congenital malformations known to be characteristic of infants born to mothers with excessive intake of BZD in early pregnancy were present in 25 of 10,646 live born infants (2.3/1,000) delivered by mothers living in the city of Gothenburg in 1985 and 1986. The maternal plasma was analyzed in 18 of these cases 1.2 to 1.5 years after the birth of the probands; eight samples (44%) were BZD positive. Of 60 controls, two maternal blood samples (3%) were positive for BZD. The difference was highly significant and suggests an association between the congenital malformation and BZD consumed during early gestation. (Laegried L et al. Congenital malformations and maternal consumption of benzodiazepines: A case-control study. Dev Med Child Neur May 1990; 32:432-441).

COMMENT. The diagnoses considered to be specific for BZD-induced congenital malformations were embryopathy and fetopathy, nervous system malformations, cleft lip and cleft