ABSTRACT

A specific pattern of malformation involving prenatal-onset growth deficiency, developmental delay, craniofacial anomalies, and limb defects is now recognized in offspring of chronic alcoholic women. Historical evidence suggests that this is not a new observation. A recent French study of 127 offspring of alcoholic mothers indicates that this specific syndrome has been recognized in other parts of the world. Many of the features of this disorder could be related to the kind of malorientation of brain structure seen at the autopsy of one patient described herein. The frequency (43%) of adverse outcome of pregnancy for chronic alcoholic women suggests that serious consideration be given to early termination of pregnancy in severely chronic alcoholic women.

A pattern of altered growth and morphogenesis, referred to as the fetal alcohol syndrome, has now been reported in 16 children, all of whom were born to severely and chronically alcoholic women who continued heavy alcohol consumption throughout pregnancy (Jones et al., '73; Jones and Smith, '73; Ferrier et al., '73; Hall and Orenstein, '74; Palmer et al., '74).

HISTORICAL PERSPECTIVE

Since the initial discrimination of the fetal alcohol syndrome historical evidence has been brought to our attention indicating that an association between maternal alcoholism and serious problems in the offspring is not a new observation. Evidence is even available from classical Greek and Roman mythology suggesting that maternal alcoholism at the time of conception can lead to serious problems in fetal development. This led to an ancient Carthaginian ritual forbidding the drinking of wine by the bridal couple on their wedding night so that defective children might not be conceived (Haggaro and Jellinek, '42). In 1834 a select committee of the British House of Commons was established to investigate "drunkenness" prior to the establishment in that same year of an Alcoholic Licensure Act. Evidence presented to that committee indicated that infants born to alcoholic mothers sometimes had a "starved, shriveled and imperfect look." In 1900 Sullivan investigated female alcoholics at the Liverpool Prison. He documented an increased frequency of early fetal death and early infant mortality in their offspring. Other investigators have found increased frequency of prematurity and decreased weight of surviving children born to chronic alcoholic mothers (Ladraque, '01; Roe, '44; Lecomte, '50; Christiaens et al., '60).

A study reported in 1967 of 127 children born to alcoholic parents was recently called to our attention by Dr. W. Lenz of Germany (Lemoine et al., '67). Abnormalities frequently noted in the children were growth deficiency of prenatal onset, an unusual facies, and a 25% incidence of malformations (in particular cleft palate and cardiac malformations). Psychomotor retardation (IQ 70) associated with "agitation" and "character disturbances" occurred often.

Animal experiments on the effects of ethanol on early morphogenesis have led...
to variable results (Sandor, '68). However, recent experiments demonstrated ethanol-induced dysmorphogenesis in chick as well as rat embryos (Sandor, '68a,b; Sandor and Amels, '71). This consisted in chicks of deformed brain vesicles and spinal cord, abnormal development of somites, and retardation of general growth.

**PATTERN OF MALFORMATION**

Features shared by the 11 children who were initially evaluated with this syndrome are summarized in figure 1. One child from each of the ethnic groups in which the fetal alcohol syndrome has been recognized are depicted in figure 2.

Prenatal growth deficiency has been more severe with regard to length than weight at birth. This is in direct contrast with most studies of generalized maternal undernutrition in which the newborn infants are underweight for their length.

Severe postnatal growth deficiency occurred in each of the 9 patients followed for longer than 1 year. The linear growth rate averaged 65% of normal whereas the average rate of weight gain was only 30% of normal despite the fact that 6 of the children were hospitalized on numerous occasions for failure to thrive, during which time adequate caloric intake was well documented, and despite the fact that 3 of them were receiving excellent foster-care. The most striking example of postnatal growth deficiency in this syndrome occurred in an American Indian girl who, at the age of 7 months had a length and weight that were in the 50th percentile for 35 weeks' gestation.

Intelligence quotients ranged from below 50 to 83 with a mean of 63.

Relative to the microcephaly, head circumference was less than the 3rd percentile for chronological age at birth in 10 out of 11 patients; and in all but 1 evaluated at 1 year of age it was below the 3rd percentile for height-age as well.

The short palpebral fissures were initially interpreted as being secondary to decreased growth of the eyes. Frank mi-