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ALCOHOLISM

Alcohol and the fetus

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ALTHOUGH concern regarding the possible adverse effects of alcohol on the developing human fetus dates back to at least the ancient Greeks, it was not until the present decade that a sufficient body of data had accumulated to allow delineation of the specific nature of the risks involved. The attention of the medical community was focused on this problem by Jones et al (1973) who noted a characteristic pattern of abnormalities in infants born to alcoholic women and termed it "the fetal alcohol syndrome". Subsequently we have come to recognize that this is the most severe end of a spectrum of abnormalities resulting from prenatal damage to the fetus by ethanol.

The fetal alcohol syndrome

The fetal alcohol syndrome is characterized by four general categories of abnormality (Hanson et al, 1976):

1. Characteristic facial appearance
2. Prenatal onset growth deficiency
3. Reduced CNS performance, including mental deficiency
4. Increased frequency of major anomalies.

This group of abnormalities may permit recognition of an affected infant shortly after birth (Jones and Smith, 1973). Indeed, in the author's experience as well as that of other investigators, the recognition of a child with this pattern of abnormalities has occasionally resulted in the secondary realization that the mother was alcoholic.

The facial features of the fetal alcohol syndrome child include a broad flat midface, a broad low nasal bridge with epicanthal folds, and a short upturned nose. The upper lip displays a relatively long philtrum and a narrow vermilion border. In many infants with this disorder the mandible is small by comparison with that of other children of the same age, but it appears relatively prominent in relation to the rest of the midfacial structures. Among the most interesting of the facial features are the relatively narrow palpebral fissures, which in some instances have been seen to be associated with small or malformed eyes. In the neonatal period the facies are frequently hirsute and many infants show mild anomalies of the auricles. These facila features are presented in **Fig. 1**.

Children with the fetal alcohol syndrome also commonly display prenatal onset growth deficiency. Furthermore, they continue to grow poorly in postnatal life. It is of interest that postnatal growth in weight is relatively slower than linear growth and results in a child who is both short in stature and disproportionately slender. Thus, a number of these children have been admitted to hospital due to "failure to thrive". Postnatal brain growth is also deficient in many such children as indicated by reduced head circumference, which is of considerable concern since it implies a reduced functional capability. Long-term follow-up studies on such children have not been completed, but a number of anecdotal observations in individual cases suggest that this growth deficiency may often be permanent.

The feature that causes the most serious concern is altered CNS performance. Of children seen by the author whose total pattern of abnormalities allowed a clear diagnosis of the fetal alcohol syndrome, the preponderance showed significant developmental delay or mental deficiency. The degree of impairment has been variable, ranging from borderline abnormalities to severe mental retardation (Streissguth, 1976). In

addition, it has been noted that these children are frequently jittery and irritable in the newborn period. The tremulousness commonly persists for months or even years and in a few instances has been found to be associated with permanent impairment of fine motor function.

Children with the fetal alcohol syndrome are also more likely to have major structural anomalies at the time of birth (Hanson et al, 1976). Cardiac defects in most cases have been mild (small ventricular or atrial septal defects), but Noonan (1976) has recently reported several children with serious cyanotic congenital heart lesions. Cleft palate has been seen in 5—15 per cent of affected children, and several children have been noted with severe ocular abnormalities including microphthalmus, coloboma of the iris or retina, and optic nerve hypoplasia. Occasional reports have mentioned axial skeletal defects, renal anomalies, and minor genital abnormalities. There also appears to be an increased frequency of positional limb deformities such as club foot and dislocated hip. Overall, 30—40 per cent of infants born to heavy-drinking mothers may have significant structural congenital anomalies (Jones et al, 1974; Quellette et al, 1976).

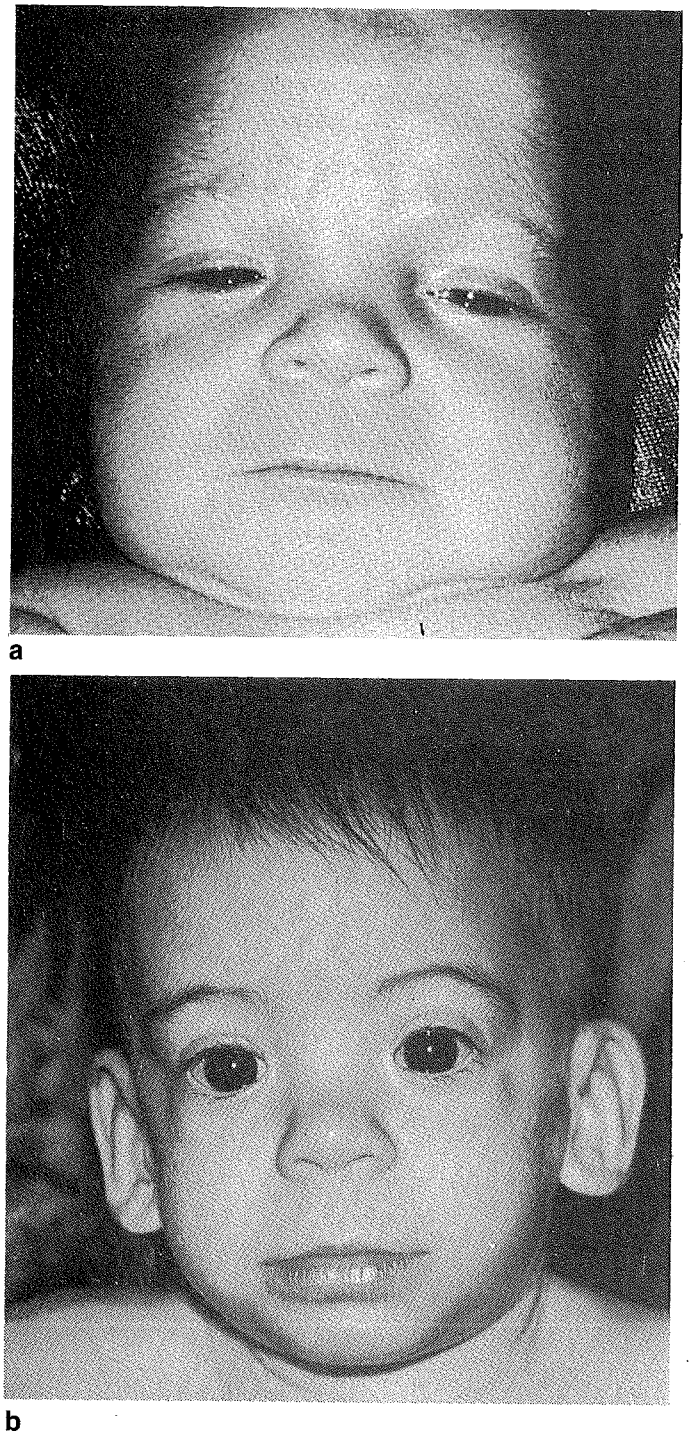

Fig. 1. **a** *Facial features of a child with the fetal alcohol syndrome at one week and* **b** *at one year of age. Note the narrow palpebral fissures, epicanthal folds, short nose with broad low bridge, flat midface, and long philtrum with narrow vermilion border.*

Epidemiological aspects

The association between maternal alcohol intake and outcome of pregnancy is strongest at the severe end of the drinking spectrum. Jones et al (1974) studied this aspect using data from the Collaborative Perinatal Project of the National Institute of Neurological Disease and Stroke. In this study, 17 per cent of infants born to severe chronic alcoholic women failed to survive the newborn period. Among the remainder, 41 per cent had an IQ below 80 at 7 years of age. Overall, at least 33 per cent of the surviving infants had sufficient characteristics noted in their medical records to be clearly classified as having the fetal alcohol syndrome. In a more recent study of heavy-drinking women from the Boston area, only two of 27 infants of women who drank heavily throughout pregnancy were considered to be totally normal (Rosette, 1977); 41 per cent of the infants had significant congenital anomalies and in 67 per cent growth was abnormal.

These observations obviously suggest that infants born to chronic alcoholic mothers are at high risk of serious congenital abnormalities, but until recently it has not been clear whether lower levels of alcohol consumption during pregnancy also present a risk to the fetus. Little et al (1976) have reported results that suggest that an average daily alcohol consumption of as low as 1 oz could be associated with significant growth impairment during prenatal life. More recently, we have reported the findings of a prospective study of 1500 pregnant women (Hanson et al, 1977) which suggest that 10 per cent of infants born to women drinking between 1—2 oz of absolute ethanol per day during the earliest part of pregnancy have recognizable alterations of growth and morphogenesis. The implications of these findings for future growth and performance in this group of children are not clear, and concern has been expressed that they may show neurological impairment on later follow-up.

It is not yet clear whether the pattern of maternal drinking represents an additional risk factor. Limited

evidence suggests that fetal outcome is most strongly correlated with the level of drinking during the earliest stages of pregnancy (Hanson et al, 1977). Recently, Clarren et al (1977) have reported neuropathological observations on brains of infants born to women who drank heavily during pregnancy. These authors evaluated 14 brains of human infants exposed in utero to variable quantities of alcohol. Brain malformations were found in five of six infants whose mothers at least occasionally consumed five or more drinks at a time during pregnancy. The brain malformations observed consisted of severe disturbances of neuronal migration, which were similar to those seen in two infants born to serious chronic alcoholics. Of particular interest is the observation that the average daily alcoholic intake of one of the mothers was not sufficiently high to have placed her in a high risk drinking category by the usual criteria although she was regarded as being a binge drinker. These observations raise the possibility that maternal binge drinking may be an additional risk factor for the fetus.

Studies in experimental animals

Although the foregoing studies clearly establish a strong relationship between excessive maternal alcohol intake during pregnancy and fetal outcome, a number of questions have been raised regarding the pathogenesis of the abnormalities observed. It has been suggested that maternal malnutrition, smoking, and concurrent drug abuse may all represent confounding factors which contribute to the problems seen in babies born to drinking mothers. A resolution of these concerns for man is not yet totally possible, although animal studies strongly implicate ethanol as a crucial aetiological factor.

In a series of rodent experiments Chernoff (1975) has produced an animal model of the fetal alcohol syndrome which displays striking similarities to the human findings. These data also suggest that it is ethanol rather than one of its metabolites which somehow impairs fetal growth and morphogenesis. Two groups of workers have confirmed these results in rodents (Tze and Lee, 1975; Randall et al, 1977) and numerous authors have found similar results in other experimental animals (Sandor and Elias, 1968; Sandor and Amels, 1971; Ellis and Pick, 1976).

Paternal alcoholism

The possibility that heavy paternal alcohol consumption might affect the fetus has also been the subject of speculation. A limited amount of animal data raises the possibility that alcohol might be a mutagen (Badr and Badr, 1975) and one study has

suggested that the chromosomes of alcoholics show a significant increase in aberrations (Obe et al, 1977). However, even if these findings were confirmed they would not account for the high frequency of abnormalities observed in the offspring of maternal alcoholics. Nor would we expect to find any consistent pattern of abnormalities in such children under these circumstances. Thus it seems clear that the most serious and consistent abnormalities among infants born to alcoholics are associated with maternal drinking, thereby implying a direct effect of ethanol on the fetus.

Clinical implications

The foregoing data have several important implications for clinicians. First, it is imperative that physicians who care for pregnant or potentially pregnant women recognize that alcohol is a dangerous drug, not only for the mothers but also for their babies. Thus, a careful history of maternal alcohol intake should be a part of every new prenatal evaluation. Mothers should be cautioned against excessive alcohol consumption at any time in pregnancy, and those who are found to be drinking heavily should be warned of the risks to their infants. In some cases the risk may be sufficiently high to warrant consideration of termination of pregnancy.

Secondly, if current findings, which suggest that drinking behaviour in the earliest part of pregnancy is a special hazard, are confirmed an additional dilemma will be posed for physicians and mothers. Women are frequently unaware that they are pregnant for the first several weeks of gestation and there is thus a substantial hazard of unwitting damage to the fetus. At the present time we would suggest that women who are considering a pregnancy or are doing nothing actively to prevent a pregnancy should avoid excessive alcohol intake at any time. It has not been established that any level of alcohol intake is totally safe for the fetus.

Thirdly, if current trends in social drinking continue this problem may become more frequent in the future as an increasing number of young women and children are exposed to alcohol (Demone and Wechsler, 1977). Thus the most important mode of controlling this avoidable tragedy would seem to be the early education of school-age children with regard to the hazards of alcohol and other dangerous drugs.

Finally, it is important for paediatricians to appreciate that the fetal alcohol syndrome may be one of the most frequent recognizable causes of mental deficiency. The identification of affected children has several potential advantages including the more appropriate use of medical facilities in the evaluation of problems of growth and development, the early recognition of infants at high risk for serious congenital anomalies, and the recognition of a mother at substantial risk for problems in future offspring. Whether or not the developmental problems identified in such children might be amenable to early treatment is still unknown.

SUMMARY

Current data clearly point to an association between chronic maternal alcoholism and serious morphological and developmental abnormalities in the fetus. When these abnormalities are severe the condition is recognizable as the fetal alcohol syndrome. However, this represents only the most severe end of a spectrum of abnormalities, some of which may be found in a proportion of infants exposed to lesser amounts of alcohol during pregnancy. Alcohol is an avoidable hazard for the fetus, but only through increased awareness by the medical community and improved education of the lay public may we hope to control this problem.

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