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The Fetal Alcohol Syndrome*

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A recognizable dysmorphic syndrome probably represents one aspect of a continuum of "reproductive casualties" associated with alcohol consumption during pregnancy. Reasons are offered for believing that the fetus, especially its brain, is vulnerable throughout pregnancy to the adverse effects of alcohol and resulting minor, but significant intellectual deficits may be overlooked.

Introduction

Although the adverse effects of alcohol on fetal development may have been recognized since Biblical times (Judges, Chapter 13, v. 7) and emphasized in a report to Parliament by the Royal College of Physicians in the early eighteenth century (cited by Woollam)[1], it is only in the last decade that serious evaluation of the epidemiology of alcohol embryopathy has been undertaken, stimulated largely by Smith and his colleagues in Seattle,[2,3,4] and Ouelette and her colleagues in Boston.[5]

The main identifying features of the fetal alcohol syndrome (F.A.S.) as listed by Smith and others are shown in Table 1.

The Specificity of F.A.S.

In trying to establish the specific identity of this syndrome, there are three crucial questions to be answered:

(1) Does the syndrome occur in the offspring of mothers who have not been exposed to alcohol before or during pregnancy?

(2) Is there a critical time and intensity of exposure to alcohol?

(3) Does the intensity of the syndrome vary with the amount of alcohol exposure – in other words, is there a "forme fruste" of the fully developed syndrome with lesser amounts of alcohol exposure?

I think the answer to the first question is an emphatic no, although I recognize that there are dangers inherent in the self-fulfilling character of the diagnosis, in so far as one would only identify the condition confidently if there was evidence of maternal alcohol consumption. Writing as someone who has a daily professional need to identify dysmorphic syndromes, I do not think I have failed to recognize the stigmata of F.A.S. in children whose mothers have not been exposed to alcohol. I therefore think the syndrome is specific.

To the questions when? and how much? one cannot give a certain answer. It is notoriously difficult to estimate daily alcohol consumption accurately from information given by heavy drinkers themselves. Estimates by Clarren and Smith[4] suggest that F.A.S. is seen in the

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TABLE 1. Clinical features of the fetal alcohol syndrome

	Affected/observed (%)
Growth and performance	
Prenatal growth defect	38/39 (97)
Postnatal growth defect	37/38 (97)
Microcephaly	38/41 (93)
Mental subnormality	31/35 (89)
Inco-ordination	28/35 (80)
Craniofacial	
Short palpebral fissures	35/38 (92)
Midfacial hypoplasia	26/40 (65)
Prominent epicanthic folds	20/41 (49)
Limbs	
Abnormal palmar creases	20/41 (49)
Joint abnormalities (mostly minor)	17/41 (41)
Miscellaneous	
Cardiac (mostly septal defects)	20/41 (49)
External genitalia (minor)	13/41 (32)
Haemangiomata	12/41 (29)
Pinnae (minor)	9/41 (22)

offspring of mothers who have consumed the equivalent of 90 ml of absolute alcohol or more daily, and the nature of the abnormalities implies that the critical period for dysgenesis is in the first trimester; one cannot assume, however, that smaller intakes of alcohol, or that exposure during the later stages of pregnancy do not have an adverse effect on fetal brain growth and differentiation.

And now to the third question. It is a criticism of the emphasis placed on the definition of F.A.S. as a specific syndrome that this may have diverted attention away from an appreciation of wider problems arising from alcohol consumption during pregnancy.[5] The apparent rarity of F.A.S. in the United Kingdom (Smithells,[6] quoting an informal survey among fellow members of the British Paediatric Association, has heard of only 5 cases) may encourage the view that the problem of alcoholism in pregnancy is negligible here. Other evidence suggests that there may be a continuum of fetal morbidity, of which F.A.S. is one extreme. For example Shaywitz *et al.*[7] reported that out of a total of 87 children referred to an assessment unit for behavioural and learning disorders in the U.S.A., there were 15 whose mothers drank heavily during pregnancy. The ages of these 11 boys and 4 girls ranged from $6\frac{1}{2}$ to 18 years, and their I.Q.s were from 82 to 113 and were thus in the average range. All had significant, and for some, substantial learning difficulties. The heights and head circumferences of 9 of them were less than the 10th percentile. Birth weights ranged from 1580 to 3150 g with a median of 2213 g, and the children when seen showed a continuum of mostly minor dysmorphic features. Although it could be argued that some or all of the learning problems may have reflected the unsatisfactory nurturing conditions which these children may have experienced throughout childhood, it would be surprising if the fetal brain, which is vulnerable to other insults throughout pregnancy, was not also similarly susceptible to neurotoxic effects of alcohol.

Equally disturbing is the report of decreased birth weights among infants whose previously alcoholic mothers abstained during pregnancy.[8] In an extensive prospective study in Boston, Ouelette *et al.*[5] were *not* able to identify a syndrome among the infants of mothers whose daily alcohol consumption was equivalent to 45 ml absolute alcohol or more.

However, there was a consistent pattern of low birth weights, neurodevelopmental abnormalities, and a variety of congenital abnormalities. Five out of 42 infants of heavy-drinking mothers were microcephalic, compared with one out of 274 offspring of mothers who either did not drink alcohol at all, or who consumed less than 45 ml absolute alcohol daily.

It must be acknowledged that epidemiological studies in this field are difficult – mothers attending for ante-natal care are self-selected, and control subjects must be carefully matched for social class, native intelligence, spouse's intelligence, smoking habits, nutritional states, drug-taking, to name but a few factors influencing the outcome of pregnancy. If, as the Boston study[5] suggests, there is a continuum of defects resulting from fetal exposure, it is unlikely that there is a well-defined "safe" threshold of consumption, nor is the fetal alcohol syndrome likely to be a discontinuous phenomenon. The fact that there is no unequivocal evidence that lesser degrees of alcohol exposure cause harm to the fetus is more a reflection of the methodological difficulties mentioned earlier than of the absence of any such effect.

Mechanism of Action

Various animal studies have confirmed that alcohol easily crosses the placenta and achieves a concentration in fetal blood similar to that in the parent.[9] Acetaldehyde, one of the important degradation products of alcohol, is very poorly metabolized by the fetus in the first trimester and could affect morphogenesis as late as the third or fourth month of gestation.[10] It has been suggested, largely on evidence of fetal abnormalities after irregular drinking, that there is a critical period when abnormalities are particularly likely to occur. A similar suggestion emerged from a study of the increased frequency of spontaneous abortions in drinking mothers. These workers postulated that acute fetal poisoning led to death and later abortion.[11] Thus it is possible that irregular heavy drinking could be as potentially harmful as sustained exposure.

Prevention

Notwithstanding the earlier suggestion that there is increased morbidity among the offspring of alcoholic mothers who abstained during pregnancy, there is evidence that abstention may minimize the effects on the fetus. At the end of the last century, in reporting the frequency of mortality and moribidity in the offspring of women imprisoned in Walton Gaol, Liverpool, Sullivan reported that several alcoholic women who had severely affected infants, later bore apparently healthy children when forced to abstain.[12,13]

Ideally, the abstention should be undertaken before, and perhaps several weeks or months before conception. But we obviously cannot dissociate this from the question of alcohol dependence in society generally.

Genteel publicity and earnest exhortation are unlikely to have a lasting impact – in the 12 years that elapsed after "Outraged" of Surbiton protested at the affront to public decency of the Health Education Council's posters showing a naked pregnant woman smoking, the proportion of mothers smoking during pregnancy had not altered significantly.

Pending more intensive educational programmes, and a more consistent example by a far-from abstemious medical profession, we may have to allow a very poor compromise, that heavy drinking is a lawful ground for termination of pregnancy.

Addendum

In an important letter with accompanying photographs it has been claimed that a syndrome indistinguishable from the Fetal Alcohol Syndrome occurs in the offspring of mothers with phenylketonuria.[14] It has also been suggested that because alcoholic mothers are zinc depleted during pregnancy this may be an important determinant of the F.A.S.[15]

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