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CLINICAL

MATERNAL DRINKING AND THE OUTCOME OF PREGNANCY: Implications for Child Mental Health

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Research since identification in 1973 of the fetal alcohol syndrome indicates that offspring of alcoholic women who drink heavily during pregnancy are at high risk for physical and mental deficiencies, and that even "social drinking" during pregnancy may have detrimental effects on birthweight and behavior of infants. While further research and remediation efforts are needed, primary prevention and active intervention in counseling and obstetrical clinics seem clearly and urgently called for.

Fetal alcohol syndrome was first identified in 1973 in a paper [10] by a team of Seattle investigators who described eight children with a similar pattern of growth deficiency, altered morphogenesis, and mental deficiency. All of these children's mothers had been chronic alcoholics and drinking heavily during pregnancy. It was suggested that the exposure to alcohol *in utero* was the primary cause of their growth deficiency, malformation, and retardation. A second paper [9] described two more cases identified at birth, and labeled the disorder fetal alcohol syndrome. The identification of a *specific* pattern of malformation and the *labeling* of the syndrome was an important step in bringing attention to this tragic and preventable form of mental deficiency. Up until this time, most health professionals had attributed the learning and

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developmental problems often found in children of alcoholics to a disruptive home life and poor caretaking. The work on fetal alcohol syndrome suggests that, in children of alcoholic mothers, the primary damage may occur *in utero*.

This was by no means the first report that alcohol ingested during pregnancy could be harmful to the developing fetus. In ancient Carthage, there was a prohibition against drinking on the wedding night for fear of producing a defective child.[12] In the 18th century a report to parliament noted that children of alcoholic mothers often had a starved, shriveled and imperfect look,[12, 39] and, in 1899, Sullivan [37] studied 120 female drunkards in the Liverpool jail and reported an unusually high incidence of perinatal mortality in their offspring. Unfortunately, these early warnings were not followed up by empirical studies, and even as late as the 1940s and 1950s government reports and books on pregnancy claimed that there were no known ill effects of alcohol to the fetus.[36] An exception to these reports was the work of a French investigator, Lemoine,[16] who in 1968 examined 100 children whose mothers were alcoholic and found them to have retarded development and a characteristic appearance similar to that described later by Jones and Smith [9] in their description of the fetal alcohol syndrome. Unfortunately, Lemoine's work remained unknown outside of France until recently.

SYNDROME CHARACTERISTICS

Children with fetal alcohol syndrome are not grossly malformed or grotesque, but they are very small both in height and weight, and have head circumferences below the third percentile.[7, 12, 23]

Children with fetal alcohol syndrome have a characteristic facies with short palpebral fissures as the most differentiating feature, and often have a flattened nasal bridge and epicanthic folds. A flattening of the mid-face (maxillary hypoplasia), mild abnormalities of the external ear, and a narrow upper lip are other less frequent anomalies. Cardiac malformations occur in about 40% of cases (primarily auricular septal defect, followed by ventricular septal defect).[3, 7]

Mental deficiency, ranging from borderline to severe, has been found in most such children [10, 35, 36] and in some children of alcoholic mothers who do not have the physical characteristics of the syndrome.[11]

Since the initial description of the fetal alcohol syndrome there have been numerous reports in the medical literature from around the world, confirming the dangers of maternal alcoholism to the developing fetus, and describing new cases of fetal alcohol syndrome.[2, 23, 36] It is now very clear that the fetal alcohol syndrome is not an isolated Seattle anomaly, but that it is found anywhere in the world where alcoholic women are having children.

The primary damage to the child clearly occurs *in utero*; children who have been raised entirely in excellent foster homes have remained as affected as those raised by their own mothers. The type of malformation that occurs suggests that structural damage began very early in pregnancy, clearly during the first trimester.[12] Affected children have been born to alcoholic women of all races who were ingesting all types of liquor and to mothers who did not take other drugs or smoke. Alcohol alone, if ingested in large enough amounts during pregnancy, appears to

produce the type of damage to the fetus that has been termed fetal alcohol syndrome.

ANIMAL MODELS

In the past few years, a number of animal studies have been carried out on the effects of alcohol on the fetus.[6, 14, 15, 18–20, 27–30, 33, 36, 38] Despite the inevitable limitations of animal studies in terms of generalizability to humans, animal studies do have the admirable virtue of control over experimental conditions that can never be obtained with humans. There should be no discrepancy, for example, between the amount of alcohol reportedly taken during pregnancy and the amount *actually* taken. Likewise, there should be no contamination of alcohol with other ingestants of known or unknown teratogenic properties. The use of pair-fed controls keeps nutrition constant across groups. Food intake is easily controlled, and outcome variables can be obtained at will.

To date, there is an animal model of fetal alcohol syndrome in chickens,[36] mice,[6, 14, 27, 28, 36] rats,[20, 36] guinea pigs,[36] and zebra fish.[15] At least one study [14] shows a dose-response curve, with fetal death (resorbtions) occurring in response to the highest maternal doses of alcohol and varying degrees of growth deficiency and malformation occurring with lower doses. The use of pair-fed controls in animal studies has clarified the role of adequate nutrition in studies on the intrauterine effects of alcohol.[20, 28] It is now clear that even in the presence of adequate nutrition during pregnancy, maternal ingestion of alcohol in experimental animals can produce growth deficiency, malformation, and increased stillbirths in the offspring. The effects of discrete doses of alcohol administered during specific stages of intrauterine development are still being studied. However, it is of particular interest that Randall [27] reported that lower doses of alcohol administered to mice in early pregnancy produced the same type of malformations as the heavier doses, only the frequency of occurrence of the malformations being decreased with lower doses.

Likewise, the study of behavioral aberrations in surviving animal offspring continues. There are some indications from rat studies that animals receiving high levels of intrauterine exposure to alcohol are more emotional as adults,[38] and are significantly inferior in learning ability as pups [20] and adults.[38] There has also been one recent study showing delayed mylenation of the fetal brain in offspring of rats receiving alcohol throughout pregnancy.[30] Studies by Rawat [29] showed decreased protein synthesis in fetuses of alcohol-fed pregnant rats and in suckling offspring of alcohol-fed mother rats.

MENTAL HANDICAPS

Most reports of the fetal alcohol syndrome that have appeared in the literature have talked of some degree of developmental delay or impaired functioning, if they have mentioned the performance of the children at all.[3, 16, 36]

Mental deficiency, in varying degrees, is probably the most debilitating aspect of the fetal alcohol syndrome. One study [11] utilized data from the Perinatal Collaborative Project, which was gathered ten to fifteen years ago at twelve hospitals across the United States on a sample of 60,000 pregancies and follow-up studies on the offspring. Unfortunately, the women had not been systematically queried regarding their alcohol consumption. However, 23

women were labeled as chronic alcoholics, with enough supporting data in the medical record to make the diagnosis seem likely. We were able to find two carefully matched controls for each alcoholic mother, matching on race, age, education and parity of mother, SES of head of household, and geographical region of delivery. The sample was predominantly a poorly educated, lower-SES group of whom 50% were nonwhite.

The findings, comparing the offspring of the alcoholic mothers to offspring of matched controls, were startling: offspring of alcoholic mothers had a seventeen percent perinatal mortality rate, compared to two percent of the controls. One-third of the surviving offspring of alcoholic mothers had enough features listed on the medical record to be retrospectively classified as fetal alcohol syndrome. But most striking of all, when given the WISC at age seven, 44% of the survivors had IQ below 79, compared to eleven percent of the controls.

The mean IQ of the offspring of alcoholic mothers was 81 at age seven, compared to IQ 95 for matched controls. Not only did these children of alcoholic mothers have significantly *lower* intelligence at seven years, but they were significantly behind their matched controls on tests of academic achievement, reading, arithmetic, and spelling. It is important to remember that these children were mostly *not* children with the physical characteristics of fetal alcohol syndrome. Intellectual deficits were found in 44% of these children of alcoholic mothers, often even in the *absence* of the physical characteristics of the syndrome.

At the University of Washington, we have recently completed a study of psychological functioning in twenty children referred clinically, all born to chronically alcoholic mothers and all with a diagnosis of fetal alcohol syndrome.[35] These children range in age from ten months to 21 years and were all given age-appropriate individually administered tests of mental or intellectual functioning. The average IQ of these children was 65 and most fell in the mildly retarded range.

Because the diagnosis of fetal alcohol syndrome involves a pattern of malformations, some children are more severely affected than others. As might be expected, there is some relationship between the degree of dysmorphogenesis and the level of intellectual functioning. The ten children who were the most severely affected also had a lower average IQ than the more moderately affected children, while those with the mildest syndrome features had the highest average IQs. However, some children with only mild physical features of fetal alcohol syndrome had considerable mental handicap. Although a positive relationship clearly exists between severity of diagnosis and degree of mental deficiency, one is not fully predictable from the other.

On the basis of these and other clinical studies, we feel that the prognosis is *not* good for children with severe manifestations of the syndrome and that even those children with mild degrees of dysmorphogenesis may have sustained bain damage prenatally that is only apparent as the child matures.

The limiting nature of clinical studies should, of course, be pointed out. Clinical studies such as these can never reflect true population parameters and are subject to whatever sampling biases are operative in the referral procedure. Obviously, children of alcoholic moth-

ers who are neither dysmorphic nor functioning poorly do not get referred. There are probably many more children with mild features of fetal alcohol syndrome or with borderline mental deficiency who are never referred, and these are best studied through prospective studies such as those presently underway at the University of Washington.

REMEDIATION

Several other factors are important to consider in making prognostic statements regarding intelligence in fetal alcohol syndrome.

1. What about the role of the environment provided by the alcoholic attainment? Are these children not handicapped by the unpredictable environment provided by the alcoholic mother? Some of our most retarded subjects have been raised entirely in excellent foster homes; we believe the *primary* damage to the central nervous system occurs *in utero*. In one study we did find somewhat, but not significantly, lower IQ scores in children who had remained with their alcoholic mothers through the age of seven years.[11] However, the number of subjects studied was very small and nothing was known about the circumstances of maternal absence in the child rearing. It may be that the critical variable is not whether the child remains with its natural mother, but whether the natural mother continues to drink. Longitudinal studies of larger numbers of childern are clearly needed. One would anticipate a compounding effect in terms of lowered performance for children who are both brain damaged and raised in disruptive and disorganized home environments.

Certainly the environment plays an ameliorating role in any child's development and the same is true for children with fetal alcohol syndrome. On the other hand, we have known foster mothers to give up in despair because they could not significantly improve the intellectual attainment of children with fetal alcohol syndrome. We believe a more realistic goal is to work with each family in terms of achieving optimal development for its own child and not to expect environmental miracle cures in children who have sustained significant intrauterine damage.

2. What about the role of specialized school settings, infant stimulation, etc.? We believe that each child should be given every opportunity to develop to his own fullest potential, and we encourage the best possible remedial experience for each child. However, we find it unlikely, based on our experiences so far, that these programs will make *dramatic* changes in the child with severe fetal alcohol syndrome, although in varying degrees they may help individual children function better. At the University of Washington, we have an infant stimulation program based on behavioral modification techniques and drug therapy, especially for children with fetal alcohol syndrome. In the one child we have studied most closely (IQ about 45), some reduction in hyperactivity was achieved but no change in IQ level was apparent after the first year of attendance.[1]

In children who are more mildly affected, special education placements have often been very helpful in providing the more individualized instruction they need. Hyperactivity is a frequent but not constant behavioral concommitant of fetal alcohol syndrome. For such children, specialized educational placement is often essential if they are to learn to capacity.

3. What about the possibility that the

children will later catch up intellectually? Are they just slow starters who will outgrow their deficits? We find this unlikely but obviously the only way to be sure is to follow a sample of children through time and study how they turn out. We are presently engaged in a follow-up study of all children with fetal alcohol syndrome that we have seen over the past three years.

We have seen one nineteen-year-old with fetal alcohol syndrome, from a well-educated, middle-class family, given many good educational experiences; his IQ at age nineteen was still only 57 despite some steady gains over the years. Despite his good genetic endowment and excellent environment, he will always be mentally handicapped and need a sheltered environment.

We believe the primary time for prevention is before the fact. The message must be spread to all women that heavy alcohol use during pregnancy may result in permanent impairment to their babies.

EFFECTS OF SOCIAL DRINKING

Once the work on fetal alcohol syndrome was publicized, the question was frequently asked: If chronic maternal alcoholism can produce fetal alcohol syndrome, then what is the consequence of more moderate levels of alcohol consumption during pregnancy?

We are familiar with five studies on the effect of alcohol use during pregnancy on birthweight and gestational age.[13, 17, 22, 26, 31] The only study with negative findings [26] used a very gross measure of alcohol consumption (drinking vs. non-drinking) and it is unlikely that this is a sensitive enough measure to be meaningful.

A recent study in France on 9000 pregnant women showed a significantly decreased birthweight in offspring of mothers ingesting over 1.6 ounces of absolute alcohol daily [13] even when other risk factors associated with higher alcohol use were controlled for. A study carried out in Seattle [17] on several hundred middle-class pregnant women in a prepaid medical program, reported a similar finding even when maternal smoking, as well as mother's age, height, parity, and gestational age and sex of infant were controlled for. Maternal alcohol use during the six months prior to pregnancy and during the eighth month of pregnancy were significantly related to birthweight of offspring. The critical level of alcohol was one ounce of absolute alcohol consumed on an average daily basis, which translates to two drinks per day, on the average. Mothers who were both heavy drinkers and heavy smokers had babies who were lighter weight than would be predicted for either substance alone. A retrospective study of birthweights of children born to patients in an alcohol treatment program showed a similar decrement compared to controls.[31] A recent prospective study of 5000 pregnancies in Germany [22] found moderate to high levels of alcohol consumption during pregnancy was related to shorter gestational ages in offspring after controlling for other relevant variables including maternal smoking.

Although birthweight and gestational age are interesting and easily obtained parameters having some relationship to overall health of offspring, individual assessments of children of heavy drinking mothers should provide more definitive results on the outcome of the pregnancy. Two prospective studies are presently underway in this country in which maternal alcohol use during pregancy is being studied in relation to

a variety of individually assessed outcome variables in the offspring.

At Boston City Hospital, a team of investigators has been interviewing pregnant women at their first prenatal visit and studying their offspring shortly after delivery. The sample of 559 women is largely poor, nonwhite, and single; ten percent have been identified as heavy drinkers during pregnancy. This proportion of heavy drinkers is five times higher than the proportion of heavy drinkers in our Seattle studies; in addition, the Boston inner-city mothers who are identified as "heavy drinkers" report a much higher average daily intake of absolute alcohol compared to our Seattle mothers, who are predominantly middle class. Thus, the sample being studied in Boston is clearly a high risk sample, on demographic background as well as alcohol use during pregnancy.

Two types of findings have been reported from the Boston group to date: 1) Examinations by a pediatric neurologist indicate that heavy alcohol use during pregnancy is associated with intrauterine growth retardation, increased jitteriness and hypotonia, and presence of major congenital malformation in the infants.[25] 2) Pilot studies on twelve infants have shown disturbances in the rythmicity of sleep patterns in the four offspring of heavy drinking mothers compared to babies of nondrinking controls.[32]

In Seattle, at two large hopsitals, one a prepaid medical program and the other the University Hospital, we are also studying the effects of social drinking on the outcome of pregancy. Our sample is predominantly white, middle class, and fairly well educated. All available pregnant women at these two hospitals who were in prenatal care by the fifth month of pregnancy were interviewed intensively regarding their ingestion habits. Seven percent of this sample were heavy drinkers in the month prior to pregnancy, and two percent were heavy drinkers during the first five months of pregnancy, using one ounce or more of absolute alcohol per average day as the criteria of a heavy drinker. Altogether, 80% of the women interviewed drank at least some alcohol during pregnancy. Smoking during pregnancy was much less common. Only 25% of the mothers smoked during pregnancy, but those who did smoke tended to smoke heavily; eleven percent of the sample were heavy smokers (using $\geqq$ 16 mg. nicotine per day as the criterion).

In this study, 500 offspring were selected for a follow-up cohort: 250 infants born to the heaviest drinkers and smokers, and 250 controls born to nonsmokers and infrequent drinkers or abstainers. Subsets of these infants were given five independent neonatal examinations prior to discharge, including the Brazelton Neonatal Behavioral Scale, naturalistic observations of sleep/wake and activity, two types of operant learning paradigms, operant sucking and operant head turning, and dysmorphology examination. All examinations were conducted blind and by different groups of examiners. Preliminary findings from these neonatal studies indicate a variety of alcohol-related outcomes: two of the infants were felt to have the characteristics of fetal alcohol syndrome and nine others had partial features.[8] These findings were significantly related to maternal alcohol intake. Offspring of heavy-drinking mothers also performed significantly more poorly than did control babies on two factor scores from the Brazelton Scale: they did not habi-

tuate as readily to repetitive stimuli and they had poor muscle tone and immature motor behavior.[34] On the operant learning studies, there was a strong and significant alcohol/smoking interaction. Babies whose mothers were both heavy drinkers *and* heavy smokers performed significantly more poorly than controls and more poorly than predicted from either ingestant alone.[21] While it is not known to what extent these early behavioral and dysmorphic abnormalities will signal later developmental difficulty, this question is being addressed through an eight and eighteen-month follow-up of these 500 babies.

Neuropathology examinations of expired offspring of alcoholic and social drinking mothers has shown a characteristic type of brain abnormality that seems to be associated with maternal alcoholism as well as with the occasional consumption of five or more drinks at a time during the very early stages of pregnancy.[4]

CONCLUSIONS

The research of the past three years has clearly shown that alcohol is embryotoxic and teratogenic, and that the effects are not necessarily secondary to poor nutrition. Offspring of chronically alcoholic women who continue to drink heavily during pregnancy are clearly at risk for the fetal alcohol syndrome. Even those who do not have the dysmorphic features of the syndrome are at risk for lowered intellectual development. The most debilitating aspect of the fetal alcohol syndrome is the accompanying mental deficiency, which we believe now is primarily the result of the intrauterine exposure to alcohol.

The effects of more moderate levels of alcohol consumption are now being studied, but are not as definitive. Levels of consumption commonly called social drinking are significantly related to decreased birthweight in the offspring, as well as to a variety of behavioral deficits of unknown predictability.

Many questions remain unanswered. Although alcohol clearly crosses the placental barrier and circulates in the fetal bloodstream, the physiological mechanism through which the effect of alcohol is mediated has not been delineated. The potentiating effects of other drugs taken with alcohol has not been fully explored, and the increased incidence of children with fetal alcohol syndrome reported from the lower classes raises the question of other potentiating factors not yet well understood.

RECOMMENDATIONS

We feel that any woman who is alcoholic and of child-rearing age should stop drinking *prior* to conception and refrain from drinking during pregnancy *and* during the nursing period.

Those women who are alcoholic and already pregnant should have the opportunity to consider a termination and be advised to stop drinking. We have been surprised at how readily some alcoholic mothers can stop drinking in the interest of fetal welfare.

We suggest that the intake interview for both psychiatric and obstetrical clinics include some questions on maternal drug use during pregnancy, specifically alcohol. We hypothesize that some developmental delays, learning disabilities, and behavioral aberrations, such as hyperactivity, may be related to maternal alcohol use during pregnancy. We suggest that such children be given a full psychological or neuropsychological evaluation when a history of heavy maternal alcohol use appears, even in the absence of the characteristic physical

features of fetal alcohol syndrome in the child.

By conservative estimates there are at least one million alcoholic women in the United States,[24] many of child-bearing age. As early as the 1960s, an estimated 21% of women experienced moderate problems with drinking and four percent experienced severe problems.[40] Considering the precipitous increase in drinking and intoxication in adolescent girls over the past decade,[5] problems of fetal exposure to alcohol should not be underestimated.

Although many important research questions remain unanswered in this area, heavy alcohol use is clearly contraindicated during pregnancy. Mental health clinics and child treatment programs should not only provide counseling in this regard but should be alert to the possible cognitive effects on individual therapy patients of intrauterine exposure to alcohol.

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