

STATEMENT OF THE PUBLIC AFFAIRS COMMITTEE OF THE TERATOLOGY SOCIETY ON THE FETAL ALCOHOL SYNDROME

The following statement has been prepared by the Public Affairs Committee and approved by the Council.

Since the initial observations over 25 years ago that alcohol (ethanol) is a human teratogen (Jones et al., '73; Jones and Smith, '73), concerns regarding the prenatal effects of alcohol as a significant public health problem have been raised throughout the world. Much effort has gone into the delineation of a physical and neurobehavioral phenotype, numerous studies have focused on the birth prevalence of those phenotypes in various populations, and countless experiments have documented the prenatal effects of alcohol in a variety of animal species. Investigations into the risks of drinking small and moderate amounts of alcohol during pregnancy have been undertaken, education and prevention campaigns have been implemented, and programs to benefit affected children have been established.

Although there are numerous gaps in knowledge when considering the full spectrum of effects of prenatal exposure to alcohol, several unresolved problems relating to the diagnosis and prevention of the most severe end of the spectrum - the Fetal Alcohol Syndrome are of particular importance. The following five points describe these issues and the Public Affairs Committee's recommendations in response to each.

1. **Improved Recognition of the Fetal Alcohol Syndrome (FAS):**

With the exception of only the most severe cases, recognition that a child has been affected by prenatal exposure to alcohol is extremely difficult in the newborn period, and may remain so up to 4 years of age. Short palpebral fissures and a smooth philtrum, two of the characteristic features of FAS, are difficult to appreciate in a crying, uncooperative newborn infant. Furthermore, FAS features such as a short nose and low nasal bridge involve subjective judgements, and an additional feature, epicanthal folds, are normal in some ethnic groups. The result is that FAS goes unrecognized in the newborn period and beyond in an alarming number of cases (Stoler and Holmes, '99) and consequently children who could benefit from services may not be appropriately referred. In addition, physicians are frequently loath to initiate discussions of alcohol use during pregnancy with their patients, and pregnant women and new mothers are often unwilling to volunteer information that could suggest high-risk alcohol use. Furthermore, inability to validate maternal reports of exposure along with variability in research protocols on the way exposure information is collected, recorded and analyzed make it difficult to define high-risk patterns of alcohol use. Currently available biomarkers of alcohol exposure are not yet adequate to appropriately screen pregnant women for alcohol use or abuse (Stoler et al, '98; Bearer, '01).

- *We recommend that information regarding prenatal alcohol exposure be incorporated into the standard newborn evaluation form.* This would remind pediatricians to check the prenatal records and spend time with the mother inquiring about any exposure to alcohol, especially when infants are born small for gestational age. In those cases in which a positive history is elicited, a physical exam focused on screening for FAS should be performed.

- *We recommend that research be encouraged to develop more successful methods of eliciting disclosure of alcohol consumption information. We also recommend that researchers develop agreed-upon standards for measuring, reporting, and analyzing alcohol consumption patterns in pregnant women.*

- *We recommend that more sensitive and specific biomarkers of exposure among pregnant women be developed.* These tools and actions would provide a means of gathering and validating more accurate alcohol information during pregnancy, and in research settings would contribute to more meaningful comparisons of these data across studies. Ultimately these steps could improve the identification of women who are likely to deliver affected babies.

- *We recommend that strategies be developed to identify affected children early in life in order to direct those children into early intervention programs that can address developmental and behavioral problems at an age that can be of maximum help to them and to society.*

2. Identifying Neurobehavioral Effects Associated With Prenatal Exposure to Alcohol:

The most significant potential effect of prenatal alcohol exposure is on development of the central nervous system. Although neuropathologic data are based on a relatively small number of cases, a variety of structural defects have been described, including but not limited to defects of neuronal migration (Jones and Smith, '74), partial to complete absence of the corpus callosum (Clarren et al., '78; Coulter et al., '93; Kinney et al., '80), and cerebellar abnormalities including dysgenesis, heterotopies and agenesis of the vermis (Clarren et al., '78; Coulter et al., '93; Peiffer et al., '79; Wisniewski et al., '83). Magnetic Resonance Imaging (MRI) studies on living children exposed prenatally to alcohol have documented similar defects (Mattson et al., '92; Mattson et al., '96b).

With respect to neurobehavioral effects, a number of abnormalities have been noted. At birth, irritability and sucking-related difficulties have been reported (Coles et al., '87). During childhood, FAS children exhibit deficits on tests of attention (Nanson and Hiscock, '90; Coles et al., '97), executive functioning (Mattson et al., '98), particular aspects of visual spatial processing (Mattson et al., '96a), and new learning of both verbal and visual information (Mattson and Roebuck, '98). A mean IQ of 65 with a range of 20 to 120 has been documented in a review of individual FAS cases, while a mean IQ of 72 with a range of 47 to 98 has been reported in retrospective group studies (Mattson and Riley, '98). Unfortunately, outside of the research environment, it is not yet possible to be confident that a child's neurobehavioral problems are caused by prenatal alcohol exposure in the absence of the characteristic pattern of structural anomalies.

- *We recommend that research be focused on further attempts to delineate a behavioral phenotype characteristic of FAS. The identification of such a phenotype would support better estimates of the true public health impact of this disorder, even among children who do not have a sufficient number of structural features to meet the diagnostic criteria for FAS. This would allow neurobehaviorally-affected children to receive specific and early intervention services that they might otherwise be denied.*

3. Determining the Risks of Heavy Alcohol Consumption During Early Pregnancy:

Since the minimum amount of alcohol that can adversely affect fetal development remains unclear, it is desirable that women abstain from drinking alcohol during pregnancy. However, a high proportion of pregnancies are unplanned and/or unrecognized in the early weeks of gestation (Floyd et al., '99; Floyd et al., '99b). Early inadvertent exposures of non-alcoholic women to significant quantities of alcohol prior to the recognition of pregnancy may frequently occur.

- *We recommend that research be focused on the specific risks for adverse pregnancy outcome in women with heavy alcohol consumption that is restricted exclusively to the first 6 to 8 weeks of pregnancy. These data could be valuable in providing more accurate risk assessments for pregnant women with this pattern of alcohol consumption, and could also better define the potential benefit of prevention programs that target alcohol use in women prior to pregnancy.*

4. Risk Factors For and Prevention of the Fetal Alcohol Syndrome:

Despite the fact that FAS is the most common recognizable cause of mental retardation, no prevention program has yet successfully dealt with this problem. According to US survey data comparing the prevalence of reported alcohol consumption among pregnant women between 1997 and 1999, it is clear that educational programs designed to decrease risky drinking by pregnant women do not appear to be working. In 1997, 11.4% of pregnant women reported any drinking versus 12.8% in 1999; and frequent

drinking (defined as ≥ 7 drinks per week or ≥ 5 drinks on at least one occasion) increased from 2.1% to 3.3% over the same period (MMWR, '02).

While the reasons underlying the risky drinking behavior of women in this survey are unclear, among pregnant women who drink heavily, a number of factors that appear to confer susceptibility for having an FAS-affected child are beginning to emerge. These include maternal age over 30 (Jacobson et al., '96), low socioeconomic status (Abel, '95; Abel and Hannigan, '95), ethnic group (Native-American and African-American ethnicity) (Abel, '95; Abel and Hannigan, '95), alcohol dehydrogenase genotype (McCarver et al., '97; Jacobsen et al., '00; Viljoen et al., '01), and having had a previous child with FAS (May, '95). Others have suggested that nutritional deficiencies that are associated with alcohol abuse may be important risk factors for FAS (Dreosti, '93; Carey et al., '01).

- *We recommend that prevention programs be developed that focus on high-risk women, including those who previously have given birth to an affected baby, who are older, or who are of lower socioeconomic status. These prevention programs must be culturally specific and culturally appropriate.*
- *We recommend that research be focused on better understanding of the extent to which genetic factors play a role in the incidence of this disorder and that poor nutrition confers susceptibility for FAS.*

5. Social and Economic Factors Associated With the Prevalence and Prevention of FAS:

Social and economic factors can play a role in the prevalence of FAS and in the success of prevention programs. For example, in the United States, the prevalence of FAS is highest on some of the American Indian Reservations, areas of this country where the percentage of the population with 3 or even 4 of the identified risk factors is high. It is not known if there are genetic factors unique to Native-American Indians that confer additional susceptibility, if Native-American women consume greater amounts of alcohol as a way to escape from their impoverished and in some cases hopeless situations, and/or if factors such as poor nutrition and smoking, both of which are associated with lower socioeconomic status and with alcohol use, exacerbate the effects of heavy alcohol consumption on the fetus in such women. However it is clear that the prevalence of FAS is high in areas where poverty is endemic and alcohol consumption is part of the culture (Bingol et al., '87; Abel, '95).

Another example of the potential influence of poverty on the prevalence of FAS is seen in many of the poorer communities in the Western Cape province of South Africa (Croxford and Viljoen, '99). In a recent study, 46 of 1000 (4.6%) children in the normal first grade classes in a rural town in South Africa were documented to have FAS (May et al., '00), a rate which is 30 times higher than that found in industrialized nations in which it has been studied. In areas such as these, as in many of the Indian Reservations throughout North America, people have traditionally looked for ways to escape from their impoverished situation. Alcohol has been one legal and inexpensive method of escape that is widely used.

- *We recommend that programs designed to prevent FAS take into consideration the underlying social and economic bases of problem drinking and incorporate components that address these issues over and above the education of pregnant women. Only by looking at this problem within a broad social and economic context will it be possible to understand the reasons for drinking alcohol during pregnancy and to begin developing strategies that could prevent the Fetal Alcohol Syndrome.*

References

- Abel, E. 1995. An update on incidence of FAS: FAS is not an equal opportunity birth defect. *Neurotox and Teratology* 17:437-443.
- Abel EL, Hannigan JH. 1995. Maternal risk factors in Fetal Alcohol Syndrome: Provocative and permissive influences. *Neurotoxicology and Teratology* 17:445-462.

- Alcohol consumption among pregnant and child-bearing aged women-United States, 1991 and 1995. *MMWR Morb Mortal Wkly Rep* 2002; 51:346-349.
- Bearer CF. 2001. Markers to detect drinking during pregnancy. *Alcohol Res Health*;25:210-8.
- Bingol, N, Schuster C, Fuchs M, Iosubs, Turner G, Stone RK, Gromisch DS. 1987. The influence of socioeconomic factors on the occurrence of fetal alcohol syndrome. *Advances in Alcohol and Substance Abuse* 6:105-112.
- Carey LC, Coyle P, Philcox JC, Rofe AM. 2000. Maternal ethanol exposure is associated with decreased plasma zinc and increased fetal abnormalities in normal but not metallothionein-null mice. *Alcohol Clin Exp Res*;24:213-9.
- Clarren SK, Alvord EC, Sumi M, Streissguth AP, Smith DW. 1978. Brain malformations related to prenatal exposure to ethanol. *J Pediatr* 92:64-67.
- Coles CD, Smith IE, Falek A. 1987. Prenatal alcohol exposure and infant behavior: Immediate effects and implications for later development. *Advances in Alcohol and Substance Abuse* 6:87-104.
- Coles CD, Platzman KA, Raskind-Hood CL, Brown RT, Falek A, Smith IE. 1997. A comparison of children affected by prenatal alcohol exposure and attention deficit, hyperactivity disorder. *Alcoholism: Clinical and Experimental Research* 21:150-161.
- Coulter CL, Leech RW, Schaefer GB, Scheithauer BW, Brumback, RA. 1993. Midline cerebral dysgenesis, dysfunction of the hypothalamic-pituitary axis and fetal alcohol effects. *Arch Neurol* 50: 771-775.
- Croxford J, Viljoen D. 1999. Alcohol consumption by pregnant women in the Western Cape. *S Afr Med J* 89:962-965.
- Diekman ST, Floyd RL, Decoufle P, Schulkin J, Ebrahim SH, Sokol RJ. 2000. A survey of obstetrician-gynecologists on their patients' alcohol use during pregnancy. *Obstet Gynecol.* 95:756-63.
- Dreosti IE. 1993. Nutritional factors underlying the expression of the Fetal Alcohol Syndrome. *Annals of the New York Academy of Sciences* 678:193-204.
- Floyd RL, Decoufle P, Hungerford DW. 1999. Alcohol use prior to pregnancy recognition. *Am J Prev Med* 17:101-7.
- Floyd RL, Ebrahim SH, Boyle CA, Gould DW. 1999. Observations from the CDC. Preventing alcohol-exposed pregnancies among women of childbearing age: the necessity of a preconceptional approach. *J Womens Health Gen Based Med* 8:733-6.
- Jacobson JL, Jacobson SW, Sokol RJ. 1996. Increased vulnerability to alcohol-related birth defects in the offspring of mothers over 30. 1996. *Alcoholism Clinical and Experimental Research.* 20:359-363.
- Jacobson SW, Chiodo L, Jester J, Carr L, Sokol R, Jacobson J, Li TK. 2000 Protective effects of ADH2*3 in African American infants exposed prenatally to alcohol. *Alcohol Clin Exp Res* 24(Supplement):28A (Abstract)
- Jones KL, Smith DW, Ulleland CN, Streissguth AP. 1973. Pattern of malformation in offspring of chronic alcoholic mothers. *Lancet* 1: 1267-1271.
- Jones KL, Smith DW. 1973. Recognition of the fetal alcohol syndrome in early infancy. *Lancet* 2:999-1001.

- Jones KL, Smith DW. 1975. The fetal alcohol syndrome. *Teratology* 12:1-10.
- Kinney H, Faix R, Brazy J. 1980. The fetal alcohol syndrome and neuroblastoma. *Pediatr* 66: 130-132.
- Mattson SN, Goodman AM, Caine C, Delis DC, Riley EP. 1999. Executive functioning in children with heavy prenatal alcohol exposure. *Alcohol Clin Exp Res* 23:1808-15.
- Mattson SN, Grambling L, Delis DC, Jones KL, Riley EP. 1996a. Global-local processing in children prenatally exposed to alcohol. *Child Neuropsychology* 2:165-175.
- Mattson SN, Riley EP. 1998. A review of the neurobehavioral deficits in children with fetal alcohol syndrome or prenatal exposure to alcohol. *Alcohol Clin Exp Res* 22:279-294.
- Mattson SN, Riley EP, Jernigan TL, Ehlers CL, Delis DC, Jones KL, Stern C, Johnson KA, Hesselink JR, Bellugi U. 1992. Fetal alcohol syndrome: A case report of neuropsychological, MRI and EEG assessment of two children. *Alcohol Clinical Exp Res* 16:1001-1003.
- Mattson SN, Riley EP, Sowell ER, Jernigan TL, Sobel DF, Jones KL. 1996b. A decrease in size of the basal ganglia in children with fetal alcohol syndrome. *Alcohol Clinical Exp Res* 20:1088-1093.
- Mattson SN, Roebuck TM. 1998. Verbal and nonverbal memory in children with fetal alcohol syndrome. *Alcoholism: Clinical and Experimental Research* 22:185a.
- May PA. 1995. A multiple-level, comprehensive approach to the prevention of fetal alcohol syndrome (FAS) and other alcohol-related birth defect (ARBD). *International Journal of Addictions* 30:1549-1602.
- May PA, Brooke L, Gossage JP, Croxford J, Adnams C, Jones KL, Robinson L, Viljoen D. 2000. Epidemiology of fetal alcohol syndrome in a South African community in the Western Cape Province. *Am J Public Health* 90:1905-1912.
- McCarver DG, Thomasson HR, Martier SS, Sokol RJ, Li T.-K. 1997. Alcohol dehydrogenase – 2*3 allele protects against alcohol-related birth defect among African Americans. *J Pharmacology and Experimental Therapeutics* 283:1095-1101.
- Nanson JL, Hiscock M. 1990. Attention deficits in children exposed to alcohol prenatally. *Alcohol Clinical Exp Res* 14:656-661.
- Peiffer J, Majewski F, Fischbach H, Bierich JR, Volk B. 1979. Alcohol embryo-and fetopathy. *J Neural Sciences* 275-112-121.
- Stoler JM, Huntington KS, Peterson CM, Peterson KP, Daniel P, Aboagye KK, Lieberman E, Ryan L, Holmes LB. 1998. The prenatal detection of significant alcohol exposure with maternal blood markers. *J Pediatr* 133:346-52
- Stoler JM, Holmes LB. 1999. Under-recognition of prenatal alcohol effects in infants of known alcohol abusing women. *J Pediatr* 135:430-436.
- Viljoen DL, Carr LG, Foroud TM, Brooke L, Ramsay M, Li TK. 2001. Alcohol dehydrogenase-2*2 allele is associated with decreased prevalence of fetal alcohol syndrome in the mixed-ancestry population of the Western Cape Province, South Africa. *Alcohol Clin Exp Res* 25:1719-22.
- Wisniewski K, Dambaska M, Sher JH, Qazi Q. 1983. A clinical neuropathological study of the fetal alcohol syndrome. *Neuropediatr* 14:197-201.

--- Alcohol use among women of childbearing age – United States 1991-1999. 2002 Morbidity and Mortality Weekly Report. 51:273.

--- Errata: Vol 51, No. 13. 2002 Morbidity and Mortality Weekly Report.