

Special Section

THE LONG-TERM NEUROCOGNITIVE CONSEQUENCES OF PRENATAL ALCOHOL EXPOSURE: A 14-Year Study

Ann P. Streissguth,¹ Helen M. Barr,¹ Fred L. Bookstein,²
Paul D. Sampson,³ and Heather Carmichael Olson¹

¹Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine; ²Institute of Gerontology, University of Michigan; and ³Department of Statistics, University of Washington School of Arts and Sciences

Abstract—Prenatal alcohol exposure, at doses not generally associated with maternal alcohol problems, produces a broad array of neurocognitive deficits in offspring even in the absence of effects on growth and morphology. This report presents a summary of neurobehavioral, growth, and morphology findings from long-term follow-up of a birth cohort of 500 from a population-based study that has revealed attention, memory, and information processing deficits from birth through 14 years. Also observed (from school age through 14 years) have been problems with antisocial and delinquent behaviors, and classroom learning and behaviors; some of these problems may be secondary to earlier neurocognitive disabilities. Continuing research in behavioral and neurobehavioral teratology provides important opportunities for the neurosciences and for improved health of future generations.

In 1973, fetal alcohol syndrome (FAS) was identified as a birth defect presumed to be caused by prenatal alcohol exposure because the physical findings were observable at birth and the birth mothers of the first children so identified were chronic alcoholics (Jones & Smith, 1973). In the subsequent 25 years, alcohol has been irrefutably established as a teratogen through thousands of experimental animal studies, the whole field of neurobehavioral teratology has emerged (Riley & Vorhees, 1986), and hundreds of studies have demonstrated the comparability of the neurobehavioral findings from human and animal research on the short- and long-term consequences of prenatal alcohol exposure (Table 1; Driscoll, Streissguth, & Riley, 1990).

Although FAS has been identified as the most frequent known cause of mental retardation, clinical work proceeded slowly because of the subtleties of establishing the clinical diagnosis (Streissguth, 1997). FAS is diagnosed by the coexistence of three features: prenatal-onset growth deficiency, a characteristic pattern of dysmorphological characteristics read most explicitly in the face, and evidence of central nervous system (CNS) dysfunction. But the diagnostic process has not been readily incorporated in clinical practice, and thousands of individuals remain undiagnosed.

Hundreds of experimental animal studies have shown that the brain is the organ that is the most vulnerable to prenatal alcohol exposure (Goodlett & West, 1992) and that CNS effects can last a lifetime (Dumas & Rabe, 1994). However, no specific and unique clinical markers that are suitable for the detection of individuals with the CNS effects of prenatal alcohol exposure have emerged. The Institute of

Medicine (Stratton, Howe, & Battaglia, 1996) recently suggested the new term alcohol-related neurodevelopmental disabilities (ARND) to describe children who were prenatally exposed to alcohol and have variable CNS effects but lack the physical features of FAS. Defining ARND poses a challenge for neuroscientists and clinicians that should not go unnoticed.

The magnitude of the public-health problem posed by prenatal alcohol exposure is clear from two recent studies based on empirical and clinical methods. The first concluded that the incidence and prevalence of FAS and ARND combined is almost 1 out of 100 live births (Sampson et al., 1997). The second documented the costly secondary disabilities, such as school or job difficulties, experienced by individuals with FAS and other fetal alcohol effects as they attempt to pursue lives handicapped by primary CNS disabilities that frequently go unrecognized (Streissguth, Barr, Kogan, & Bookstein, 1997).

The present article describes findings from the Seattle Longitudinal Prospective Study (a population-based study ongoing since 1974) that demonstrate broad and variable CNS effects of prenatal alcohol in a primarily low-risk population conceived before general awareness of alcohol's adverse effects on pregnancy outcome and the later lives of children and adolescents. We propose using this accruing body of knowledge as a basis for developing tools that detect individuals affected by prenatal alcohol exposure, whatever their age.¹

METHOD

Two hospitals with demographic characteristics representative of the Seattle area were selected for study (Table 2). So that alcohol effects could be studied in the absence of competing risks, only women enrolled in prenatal care by the 5th month of pregnancy were eligible. The screening interviews from 1,529 consecutive consenting women revealed a fairly low-risk lifestyle in relation to a variety of factors that could relate to their offsprings' health, including diet, drugs, medications, caffeine, alcohol, smoking, family history, and environment. The follow-up birth cohort of approximately 500 infants represented an oversampling of the heavier drinkers and smokers from the original 1,529 mothers, along with others representing a variety of drinking patterns, including abstaining (Table 3). In this sample, 18% used marijuana (2% used other street drugs), 12% had not graduated from high school, and 8% were on welfare.

Address correspondence to Ann P. Streissguth, Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, 180 Nickerson St., Suite 309, Seattle, WA 98109; e-mail: astreiss@u.washington.edu.

1. This article extends prior reviews of this study, most recently, Streissguth, Bookstein, and Barr (1996). A full list of reports from the study is available from the senior author.

Table 1. *Comparable behavioral effects following prenatal alcohol exposure in humans and animals*

Humans	Animals
Hyperactivity, reactivity	Increased activity, exploration, and reactivity
Attention deficits, distractibility	Decreased attention
Lack of inhibition	Inhibition deficits
Mental retardation, learning difficulties	Impaired associative learning
Reduced habituation	Impaired habituation
Perseveration	Perseveration
Feeding difficulties	Feeding difficulties
Gait abnormalities	Altered gait
Poor fine and gross motor skills	Poor coordination
Developmental delay (motor, social, language)	Developmental delay
Hearing abnormalities	Altered auditory evoked potentials
Poor state regulation	Poor state regulation

Note. Reprinted by permission of the publisher from Driscoll, Streissguth, and Riley (1990).

The primary independent variable, alcohol, was assessed via a quantity-frequency-variability interview with additional questions regarding having more than five drinks per occasion, intoxications, and problems with drinking. Drinking during two time periods was assessed: during pregnancy and prior to pregnancy or recognition of pregnancy (see Streissguth, Bookstein, Sampson, & Barr, 1993, for details). The majority of mothers were white, married, middle class, and well educated, although a broad range of socioeconomic and racial groups was represented (Table 2). Heavier drinkers did not differ from the rest of the mothers in terms of nutrition, maternal weight gain, prenatal care, or other pregnancy risk factors such as diabetes, renal disease, thyroid abnormality, or rubella.

Children in the follow-up cohort were examined on the first 2 days of life, at 8 and 18 months, and at 4, 7, and 14 years. Parents

were interviewed at each examination; teacher evaluations were obtained at 8 and 11 years. All examinations were conducted blind, without the examiner knowing subjects' exposure history, living conditions, or previous scores. Follow-up has been excellent, with at least 82% of the original follow-up birth cohort included at each assessment. There has been no differential loss of heavily exposed subjects.

Data analyses from the first 4 years of life involved multiple regression analyses of single outcomes against single alcohol predictor variables. Analyses from 7 years onward have incorporated partial least squares (PLS), a method of data analysis that permits the simultaneous assessment of relations among multiple alcohol predictor scores and multiple outcome scores. PLS is better suited than multiple regression or other alternatives to the complex multifactorial data generated in human behavioral teratology studies such as ours (Bookstein, Sampson, Streissguth, & Barr, 1996). In teratology studies, a PLS analysis typically yields a dose latent variable, or LV (here, *alcohol*), and a response LV (here, *outcomes*) for each study (Sampson, Streissguth, Barr, & Bookstein, 1989; Streissguth, Bookstein, Sampson, & Barr, 1989; Streissguth et al., 1993). The specification of the pair of LVs, and their relationship, demonstrates the salience of the prenatal alcohol scores for the outcomes under consideration, and similarly, the salience of these outcomes for prenatal alcohol exposure. The alcohol LV, which is computed as a linear combination of all the prenatal dose measures, is very stable over the whole range of outcome ages examined in the present study.

Data on possible confounds were obtained prenatally and prospectively at each succeeding examination. Now exceeding 150, these variables include maternal nutrition and use of all drugs and medications during pregnancy, sociodemographic and education characteristics of the family, mother-child interactions, major life stresses in the household, childhood accidents, hospitalizations and illnesses, education experiences of the child, and many others (Streissguth et al., 1993).

All findings reported here have been evaluated in terms of potential confounds. Correlations between the many covariates in the database and the outcome LVs were examined. Then covariates associated with both the alcohol LV and the outcome LVs were examined in regression analyses to see the extent to which they altered the estimated effects of alcohol dose. Scatter plots and partial residual plots were routinely examined.

Table 2. *Maternal and household characteristics: Screening sample versus follow-up cohort*

Characteristic	Screening sample (N = 1,529)	Follow-up cohort (N = 464)
White	86%	88%
Married	87%	87%
Middle class	81%	81%
Prenatal vitamins taken during pregnancy	98%	98%
Prenatal care received by 5th month	100%	100%
Mean educational level	13.8 years	13.7 years
Mean number of children in household	1.0	0.9
Median annual income (at age 14)	—	\$45,000

Note. All statistics except for median family income reflect maternal or household characteristics at the time of the prenatal interview in 1974–1975. Number of children excludes the cohort child.

Table 3. Alcohol use by mothers (drinkers only): Screening sample versus cohort mothers

Measure of drinking	Screening sample		Cohort mothers	
	Mean	Median	Mean	Median
Drinks per day (beer, wine, liquor)				
Before recognition of pregnancy	0.8	0.4	1.6	0.8
During midpregnancy	0.4	0.2	0.6	0.3
Monthly occasions of drinking				
Before recognition of pregnancy	10.3	6.0	16.9	9.0
During midpregnancy	5.7	3.3	8.0	4.5
Average drinks per occasion				
Before recognition of pregnancy	2.1	1.5	2.5	2.2
During midpregnancy	1.9	1.5	2.2	1.8
Maximum drinks per occasion				
Before recognition of pregnancy	3.1	1.5	4.0	3.5
During midpregnancy	2.8	1.5	3.6	3.5
Percentage reporting binge drinking (5 or more drinks on any occasion)				
Before recognition of pregnancy	18.8		39.1	
During midpregnancy	12.2		24.1	

Note. The data for the screening sample ($N = 1,529$) do not include 299 mothers (20%) who abstained before they realized they were pregnant and 287 (19%) who abstained during midpregnancy. The data for the 14-year follow-up cohort ($N = 464$) do not include 124 mothers (27%) who abstained before they realized they were pregnant and 103 (22%) who abstained during midpregnancy. A drink was calculated at 0.5 oz or 15 g of absolute alcohol per day.

RESULTS

The neurobehavioral effects of prenatal alcohol summarized here have been measured in this study from the first day of life through 14 years. The observed effects of alcohol on offspring are dose dependent, generally without a threshold, and are more salient for binge-type maternal alcohol use than for other measures of use. Self-reported drinking prior to recognition of pregnancy is generally more salient for these outcomes than drinking in midpregnancy, but the two are highly correlated. The results reported are not attributable to such potential confounds as exposures to other drugs, smoking, or social and demographic factors (Streissguth et al., 1993). For details of specific analyses, see the original scientific reports from which this overview derives. Streissguth et al. (1993) lists those reports pertaining to the first 7 years of life.

This study measured three types of outcomes across the life span: neurobehavioral deficits, growth, and alcohol-related physical anomalies. At birth, all three were related to prenatal alcohol exposure. After 8 months of age, alcohol effects on height, weight, and head circumference were no longer observable (Sampson, Bookstein, Barr, & Streissguth, 1994). Alcohol-related facial dysmorphic features were detected at birth and at 4 years from "blind" clinical examinations and at 7 years from facial photographs (Streissguth, Bookstein, & Barr, 1996). By 14 years, effects of prenatal exposure to alcohol were no longer detectable in the face. Alcohol effects on neurobehavioral deficits, however, have not attenuated over time, and a rich body of data for the first 14 years of life has accrued.

On Day 1, the Brazelton Neonatal Behavior Scale was administered blind to 417 infants. Prenatal alcohol exposure was related to poorer habituation, indicating difficulty "tuning out" redundant stimuli, and to poorer response modulation (Streissguth, Barr, & Martin,

1983). Alcohol was also related to other CNS responses, including increased head turning to the left, increased tremulousness, increased hand-to-face movements, increased time with eyes open, and decreased bodily activity (Streissguth et al., 1993). On Day 2 of life, prenatal alcohol was related to longer latency to suck and lower sucking pressure obtained on a pressure-transducer measure of nonnutritive sucking (Streissguth et al., 1996). These early neurobehavioral findings indicated that even before the infants left the hospital, they had measurable effects of prenatal alcohol exposure.

At 8 months of age (but not at 18 months), prenatal alcohol exposure was related to small decrements in mental and motor development measured on the Bayley Scales of Infant Mental and Motor Development (Streissguth, Barr, Martin, & Herman, 1980). At 4 years, prenatal alcohol exposure was related to decreased attention and longer response latency on a computerized vigilance test (Streissguth, Sampson, et al., 1994), longer latency to correct errors (suggesting slower central processing time) and poorer fine motor performance on the Wisconsin Motor Steadiness Battery, poorer gross motor performance (especially on balance; Barr, Streissguth, Darby, & Sampson, 1990), and IQ decrements on the Wechsler Preschool and Primary Scale of Intelligence (Streissguth, Barr, Sampson, Darby, & Martin, 1989).

At 7 years, prenatal dose was associated with decrements on the Wechsler Intelligence Scale for Children-Revised (WISC-R), particularly Arithmetic and Digit Span subtest scores, and with arithmetic deficits on the Wide Range Achievement Test-Revised (Sampson et al., 1989). In the domain of vigilance, prenatal dose predicted deficits of several sorts in the Continuous Performance Test (CPT) vigilance scores, notably errors of commission on the AX task and standard deviation of reaction time throughout (Streissguth, Samp-

son, et al., 1994). Other consequences of prenatal exposure include poorer performance on tests of spatial memory and integration, verbal memory and integration, flexible problem solving, and perceptual motor function, and on examiners' ratings of distractibility, organization, and flexibility in problem solving (Streissguth, Bookstein, et al., 1989).

By the end of the second grade, heavier prenatal alcohol exposure was associated with an increased chance that a child would be in special programs and classes at school. The children were also rated by teachers on standardized rating scales as not well organized, lacking tactfulness, and having poor grammar, poor word recall, and poor attention in the classroom (Sampson et al., 1989). At 11 years, alcohol-related effects emerged in continuing teacher reports of processing and reasoning problems, as well as ratings of distractibility, impulsiveness, and restlessness. Prenatal alcohol exposure was also related at age 11 to poorer academic achievement, as reflected in teacher ratings (of reading, arithmetic, written expression, spelling, and overall learning) and lower national percentile scores (especially for arithmetic and total achievement; Carmichael Olson, Sampson, Barr, Streissguth, & Bookstein, 1992). Teacher ratings of classroom attention at 11 years, in the fifth and sixth grade, were predicted by the 7-year vigilance LV ($r = .36$). Teacher ratings also predicted the 14-year vigilance LV ($r = .42$). Although poor vigilance characterized some subjects across the entire exposure range, high alcohol exposure appeared to vitiate any possibility that the adolescent would score in the very best range for vigilance (i.e., make very few errors; Streissguth, Bookstein, Sampson, & Barr, 1995).

At 14 years, prenatal alcohol exposure was related to poorer performance on laboratory measures of attention, memory, phonological processing, and arithmetic (Streissguth, Sampson, et al., 1994). The same alcohol LV associated with neurobehavioral outcomes at earlier ages had highest saliences for standard deviation of reaction time and errors of commission on AX measured on CPT Vigilance, for a complex letter-cancellation test, and for a demanding spatial memory test called the Stepping Stone Maze. The attention-memory LV at 14 years correlated .67 with the neurobehavioral LV salient for prenatal alcohol exposure from birth to 7 years. Word Attack, a test thought to measure a more biological aspect of linguistic skill than reading skill, and the Arithmetic subtest of the WISC-R each revealed an approximately 1/3-SD decrement in performance at exposure levels of more than 1.5 drinks per occasion on average (Streissguth, Barr, et al., 1994). Ten out of 11 children of heavier drinkers who had low Arithmetic scores at 7 years continued to have low Arithmetic scores at 14 years.

A recent report from this study (Carmichael Olson et al., 1997) showed that prenatal alcohol exposure (essentially the same alcohol LV as discussed earlier) is related to learning and behavior problems self-reported by adolescents and observed by parents and in ratings by research examiners. These observations include projecting a subtle impression as a "bad kid" to the research examiner; antisocial and delinquent behaviors; early use of tobacco, alcohol, and other drugs; poor academic progress; partaking of special programs for the learning disabled; and low grades in mathematics. Examiners' ratings salient for prenatal alcohol exposure in these teenagers included high impulsivity and problems with organization, especially under stress—behaviors similar to those attributed to these subjects by a different set of examiners 7 years earlier. Clearly, the cognitive and neurobehavioral deficits measured earlier had an impact on classroom learning and behavior as the children matured.

SUMMARY

The remarkable 25-year history of multidisciplinary research on the effects of prenatal alcohol exposure in animals and humans constitutes the most intensive study of a teratogen ever undertaken, to our knowledge. This is fitting, as alcohol is the teratogen most frequently used by pregnant women in the Western world. The procedural and statistical methodology for examining neurobehavioral cognitive outcomes has been substantially enhanced by these research opportunities. Neurobehavioral outcomes represent the most enduring and debilitating of the three types of alcohol-related deficits initially defining FAS and reveal FAS as merely an endpoint of a continuum of untoward CNS effects in dose-response relationship to prenatal exposure. These findings persist, in the human study reported here, after adjustment for important potential confounding factors, and are compellingly supported by a superabundance of findings reported in the animal literature. The study described here is only one of several that are continuing to show enduring effects of prenatal alcohol exposure in very different populations (Autti-Rämö & Granström, 1996; Coles, 1994; Day & Richardson, 1994; Jacobson et al., 1993; Larroque et al., 1995). It is clear that no level of exposure is safe for every pregnancy. These data support the recommendation of the Surgeon General regarding not drinking during pregnancy (U.S. Surgeon General, 1981).

However, important scientific questions still remain. What will be the adult sequelae of those childhood and adolescent cognitive and attentional deficits? Will they evolve to alcohol and drug dependence and mental illness? Could such resulting secondary disabilities be preventable if these neurobehavioral birth defects are better understood and identified? Can laboratory findings be distilled into useful tools to identify individuals with ARND across the life span so that interventions can be targeted better? Will new technology and statistical advances in brain imaging reveal the biological underpinnings of these cognitive neurobehavioral deficits? The cognitive neurosciences should play a key role in understanding the subtle deviations in brain structure and function that can arise prenatally from alcohol and other teratogens.

Acknowledgments—This research has been primarily supported by U.S. Public Health Service Grant No. AA01455-01-22 from the National Institute on Alcohol Abuse and Alcoholism (NIAAA). We gratefully acknowledge the contributions of the study hospitals, Group Health Cooperative of Puget Sound and the University Hospital; the original co-investigators, Joan and Donald Martin; and the important support of NIAAA staff, especially Kenneth Warren, Laurie Foudin, and Mary DuFour. John Anzinger, Kristi Covell, Sharalyn Jackson, and Lisette Womack are thanked for technical assistance. Most important, we thank the children and families whose loyal support made this study possible.

REFERENCES

- Autti-Rämö, H., & Granström, M.-J. (1996). Effects of fetal alcohol exposure on early cognitive development. In H.L. Spohr & H.C. Steinhausen (Eds.), *Alcohol, pregnancy and the developing child* (pp. 169–182). Cambridge, England: Cambridge University Press.
- Barr, H.M., Streissguth, A.P., Darby, B.L., & Sampson, P.D. (1990). Prenatal exposure to alcohol, caffeine, tobacco, and aspirin: Effects on fine and gross motor performance in 4-year-old children. *Developmental Psychology*, 26, 339–348.
- Bookstein, F.L., Sampson, P.D., Streissguth, A.P., & Barr, H.M. (1996). Exploiting redundant measurement of dose and developmental outcome: New methods from the behavioral teratology of alcohol. *Developmental Psychology*, 32, 404–415.

Neurocognitive Consequences of Prenatal Alcohol

- Carmichael Olson, H., Sampson, P.D., Barr, H.M., Streissguth, A.P., & Bookstein, F.L. (1992). Prenatal exposure to alcohol and school problems in late childhood: A longitudinal prospective study. *Development and Psychopathology*, *4*, 341–359.
- Carmichael Olson, H., Streissguth, A.P., Sampson, P.D., Barr, H.M., Bookstein, F.L., & Thiede, K. (1997). Association of prenatal alcohol exposure with behavioral and learning problems in early adolescence. *Journal of the American Academy of Child and Adolescent Psychiatry*, *36*, 1187–1194.
- Coles, C. (1994). Critical periods for prenatal alcohol exposure: Evidence from animal and human studies. *Alcohol Health and Research World*, *18*(1), 22–29.
- Day, N.L., & Richardson, G.A. (1994). Comparative teratogenicity of alcohol and other drugs. *Alcohol Health and Research World*, *18*(1), 42–48.
- Driscoll, C.D., Streissguth, A.P., & Riley, E.P. (1990). Prenatal alcohol exposure: Comparability of effects in humans and animal models. *Neurotoxicology and Teratology*, *12*, 231–237.
- Dumas, R.M., & Rabe, A. (1994). Augmented memory loss in aging mice after one embryonic exposure to alcohol. *Neurotoxicology and Teratology*, *16*, 605–612.
- Goodlett, C.R., & West, J.R. (1992). Fetal alcohol effects: Rat model of alcohol exposure during the brain growth spurt. In I.S. Zagon & T.A. Slotkin (Eds.), *Maternal substance abuse and the developing nervous system* (pp. 45–75). San Diego: Academic Press.
- Jacobson, J.L., Jacobson, S.W., Sokol, R.J., Martier, S.S., Ager, J.W., & Kaplan-Estrin, M.G. (1993). Teratogenic effects of alcohol on infant development. *Alcoholism: Clinical and Experimental Research*, *17*, 174–183.
- Jones, K.L., & Smith, D.W. (1973). Recognition of the fetal alcohol syndrome in early infancy. *Lancet*, *2*(836), 999–1001.
- Larroque, B., Kaminski, M., Dehaene, P., Subtil, D., Delfosse, M.-J., & Querleu, D. (1995). Moderate prenatal alcohol exposure and psychomotor development at preschool age. *American Journal of Public Health*, *85*, 1654–1661.
- Riley, E.P., & Vorhees, C.V. (1986). *Handbook of behavioral teratology*. New York: Plenum Press.
- Sampson, P.D., Bookstein, F.L., Barr, H.M., & Streissguth, A.P. (1994). Prenatal alcohol exposure, birthweight, and measures of child size from birth to age 14 years. *American Journal of Public Health*, *84*, 1421–1428.
- Sampson, P.D., Streissguth, A.P., Barr, H.M., & Bookstein, F.L. (1989). Neurobehavioral effects of prenatal alcohol: Part II. Partial least squares analysis. *Neurotoxicology and Teratology*, *11*, 477–491.
- Sampson, P.D., Streissguth, A.P., Bookstein, F.L., Little, R.E., Clarren, S.K., Dehaene, P., Hanson, J.W., & Graham, J.M. (1997). The incidence of fetal alcohol syndrome and the prevalence of alcohol-related neurodevelopmental disorder. *Teratology*, *56*, 317–326.
- Stratton, K.R., Howe, C.J., & Battaglia, F.C. (Eds.). (1996). *Fetal alcohol syndrome: Diagnosis, epidemiology, prevention and treatment*. Washington, DC: National Academy Press.
- Streissguth, A.P. (1997). *Fetal alcohol syndrome: A guide for families and communities*. Baltimore: Paul H. Brookes.
- Streissguth, A.P., Barr, H.M., Carmichael Olson, H., Sampson, P.D., Bookstein, F.L., & Burgess, D.M. (1994). Drinking during pregnancy decreases Word Attack and Arithmetic scores on standardized tests: Adolescent data from a population-based prospective study. *Alcoholism: Clinical and Experimental Research*, *18*, 248–254.
- Streissguth, A.P., Barr, H.M., Kogan, J., & Bookstein, F.L. (1997). Primary and secondary disabilities in Fetal Alcohol Syndrome. In A.P. Streissguth & J. Kanter (Eds.), *The challenge of Fetal Alcohol Syndrome: Overcoming secondary disabilities* (pp. 25–39). Seattle: University of Washington Press.
- Streissguth, A.P., Barr, H.M., & Martin, D.C. (1983). Maternal alcohol use and neonatal habituation assessed with the Brazelton Scale. *Child Development*, *54*, 1109–1118.
- Streissguth, A.P., Barr, H.M., Martin, D.C., & Herman, C.S. (1980). Effects of maternal alcohol, nicotine and caffeine use during pregnancy on infant mental and motor development at 8 months. *Alcoholism: Clinical and Experimental Research*, *4*, 152–164.
- Streissguth, A.P., Barr, H.M., Sampson, P.D., Darby, B.L., & Martin, D.C. (1989). IQ at age 4 in relation to maternal alcohol use and smoking during pregnancy. *Developmental Psychology*, *25*(1), 3–11.
- Streissguth, A.P., Bookstein, F.L., & Barr, H.M. (1996). A dose-response study of the enduring effects of prenatal alcohol exposure. In H.L. Spohr & H.C. Steinhausen (Eds.), *Alcohol, pregnancy and the developing child* (pp. 141–168). Cambridge, England: Cambridge University Press.
- Streissguth, A.P., Bookstein, F.L., Sampson, P.D., & Barr, H.M. (1989). Neurobehavioral effects of prenatal alcohol: Part III. PLS analyses of neuropsychologic tests. *Neurotoxicology and Teratology*, *11*, 493–507.
- Streissguth, A.P., Bookstein, F.L., Sampson, P.D., & Barr, H.M. (1993). *The enduring effects of prenatal alcohol exposure on child development: Birth through 7 years, a partial least squares solution*. Ann Arbor: University of Michigan Press.
- Streissguth, A.P., Bookstein, F.L., Sampson, P.D., & Barr, H.M. (1995). Attention: Prenatal alcohol and continuities of vigilance and attentional problems from 4 through 14 years. *Development and Psychopathology*, *7*, 419–446.
- Streissguth, A.P., Sampson, P.D., Carmichael Olson, H., Bookstein, F.L., Barr, H.M., Scott, M., Feldman, J., & Mirsky, A.F. (1994). Maternal drinking during pregnancy: Attention and short-term memory in 14-year-old offspring—A longitudinal prospective study. *Alcoholism: Clinical and Experimental Research*, *18*, 202–218.
- U.S. Surgeon General. (1981). Surgeon General's Advisory on Alcohol and Pregnancy. *FDA Drug Bulletin*, *11*(2), 9–10.