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Prenatal Alcohol Exposure and Childhood Behavior at Age 6 to 7 Years: I. Dose-Response Effect

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ABSTRACT. *Objective.* Moderate to heavy levels of prenatal alcohol exposure have been associated with alterations in child behavior, but limited data are available on adverse effects after low levels of exposure. The objective of this study was to evaluate the dose-response effect of prenatal alcohol exposure for adverse child behavior outcomes at 6 to 7 years of age.

Methods. Beginning in 1986, women attending the urban university-based maternity clinic were routinely screened at their first prenatal visit for alcohol and drug use by trained research assistants from the Fetal Alcohol Research Center. All women reporting alcohol consumption at conception of at least 0.5 oz absolute alcohol/day and a 5% random sample of lower level drinkers and abstainers were invited to participate to be able to identify the associations between alcohol intake and child development. Maternal alcohol, cigarette, and illicit drug use were prospectively assessed during pregnancy and postnatally. The independent variable in this study, prenatal alcohol exposure, was computed as the average absolute alcohol intake (oz) per day across pregnancy. At each prenatal visit, mothers were interviewed about alcohol use during the previous 2 weeks. Quantities and types of alcohol consumed were converted to fluid ounces of absolute alcohol and averaged across visits to generate a summary measure of alcohol exposure throughout pregnancy. Alcohol was initially used as a dichotomous variable comparing children with no prenatal alcohol exposure to children with any exposure. To evaluate the effects of different levels of exposure, the average absolute alcohol intake was relatively arbitrarily categorized into no, low (>0 but <0.3 fl oz of absolute alcohol/day), and moderate/heavy (≥ 0.3 fl oz of absolute alcohol/day) for the purpose of this study. Six years later, 665 families were contacted. Ninety-four percent agreed to testing. Exclusions included children who missed multiple test appointments, had major congenital malformations (other than fetal alcohol syndrome), possessed an IQ >2 standard deviations from the sample mean, or had incomplete data. The Achenbach Child Behavior Check-

list (CBCL) was used to assess child behavior. The CBCL is a parent questionnaire applicable to children ages 4 to 16 years. It is widely used in the clinical assessment of children's behavior problems and has been extensively used in research. Eight syndrome scales are further grouped into Externalizing or undercontrolled (Aggressive and Delinquent) behavior and Internalizing or overcontrolled (Anxious/Depressed, Somatic Complaints, and Withdrawn) behaviors. Three syndromes (Social, Thought, and Attention Problems) fit neither group. Higher scores are associated with more problem behaviors. Research assistants who were trained and blinded to exposure status independently interviewed the child and caretaker. Data were collected on a broad range of control variables known to influence childhood behavior and/or to be associated with prenatal alcohol exposure. These included perinatal factors of maternal age, education, cigarette, cocaine, and other substances of abuse and the gestational age of the baby. Postnatal factors studied included maternal psychopathology, continuing alcohol and drug use, family structure, socioeconomic status, children's whole blood lead level, and exposure to violence. Data were collected only from black women as there was inadequate representation of other racial groups.

Statistical Analyses. Statistical analyses were performed using the SPSS statistical package. Frequency distribution, cross-tabulation, odds ratio, and χ^2 tests were used for analyzing categorical data. Continuous data were analyzed using *t* tests, analyses of variance (ANOVAs) with posthoc tests, and regression analysis.

Results. Testing was available for 501 parent-child dyads. Almost one fourth of the women denied alcohol use during pregnancy. Low levels of alcohol use were reported in 63.8% and moderate/heavy use in 13% of pregnancies. Increasing prenatal alcohol exposure was associated with lower birth weight and gestational age, higher lead levels, higher maternal age, and lower education level, prenatal exposure to cocaine and smoking, custody changes, lower socioeconomic status, and paternal drinking and drug use at the time of pregnancy. Children with any prenatal alcohol exposure were more likely to have higher CBCL scores on Externalizing (Aggressive and Delinquent) and Internalizing (Anxious/Depressed and Withdrawn) syndrome scales and the Total Problem Score. The odds ratio of scoring in the clinical range for Delinquent behavior was 3.2 (1.3–7.6) in children with any prenatal exposure to alcohol compared with nonexposed controls. The threshold dose was evaluated with the 3 prenatal alcohol exposure groups. One-way ANOVA revealed a significant between group difference for Externalizing (Aggressive and Delinquent) and the Total Problem Score. Posthoc tests revealed the between group differences to be significant (no and low-

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exposure group) for Aggressive and Externalizing behavior suggesting that the adverse effects of prenatal alcohol exposure on child behavior at age 6 to 7 years are evident even at low levels of exposure. For Delinquent and Total Problem behavior, the difference was significant between the no and moderate-heavy exposure group, suggesting a higher threshold for these behaviors. Prenatal alcohol exposure remained a significant predictor of behavior after adjusting for covariates. Although maternal psychopathology was the most important predictor of behavior, gender was also a significant predictor, with boys having higher scores on Externalizing (Delinquent) and Attention Problems. The amount of variance uniquely accounted for by prenatal alcohol exposure ranged between 0.6% to 1.7%.

Conclusions. Maternal alcohol consumption even at low levels was adversely related to child behavior; a dose-response relationship was also identified. The effect was observed at average levels of exposure of as low as 1 drink per week. Although effects on mean scores for Externalizing and Aggressive behaviors were observed at low levels of prenatal alcohol exposure, effects on Delinquent behavior and Total Problem Scores were observed at moderate/heavy levels of exposure. Children with any prenatal alcohol exposure were 3.2 times as likely to have Delinquent behavior scores in the clinical range compared with nonexposed children. The relationship between prenatal alcohol exposure and adverse childhood behavior outcome persisted after controlling for other factors associated with adverse behavioral outcomes. Clinicians are often asked by pregnant women if small amounts of alcohol intake are acceptable during pregnancy. These data suggest that no alcohol during pregnancy remains the best medical advice. *Pediatrics* 2001; 108(2). URL: <http://www.pediatrics.org/cgi/content/full/108/2/e34>; *Child Behavior Checklist, child behavior, alcohol-related neurobehavioral effects.*

ABBREVIATIONS. HOME, Home Observation for Measurement of the Environment; CBCL, Child Behavior Checklist; OR, odds ratio; SES, socioeconomic status; FAS, fetal alcohol syndrome.

Sixteen percent of the children born in the United States are exposed prenatally to alcohol,¹ making alcohol the most common neurobehavioral teratogen.² Whereas the earliest reports of neurobehavioral toxicity related to drinking during pregnancy were described among children of alcoholic mothers,³⁻⁵ more recent research suggested deleterious outcomes for children who are exposed prenatally to moderate amounts of alcohol.⁶⁻⁸ Jacobson and Jacobson,⁹ in their review of prenatal alcohol exposure and neurobehavioral development, suggested that even the smallest dose may adversely affect the fetus. The aim of this study was to examine the effects of low levels of alcohol exposure on child behavior. Two study hypotheses were investigated: first, that prenatal alcohol exposure would adversely affect child behavior, and second, that these effects would be observed even at low levels of prenatal alcohol exposure.

METHODS

The design of this study was historical prospective. Beginning in 1986, women who attended the urban university-based maternity clinic were screened routinely at their first prenatal visit for

alcohol and drug use by trained research assistants from the Fetal Alcohol Research Center. Annually, >2400 women were screened.

Sample

Prepregnancy and current alcohol intake was elicited to determine day-by-day alcohol intake for the periconceptional period and the 2 weeks preceding the visit. All women who reported alcohol consumption at conception of at least 0.5 oz of absolute alcohol per day and a 5% random sample of lower level drinkers and abstainers were invited to participate so that we could identify the associations between alcohol intake and child development. More than 90% of women who sought prenatal care at this site were black. Therefore, because of inadequate representation of other racial groups, data were collected only from these black women. Potential participants of this child outcome study were the singleton children born to these women who had been screened extensively during pregnancy by research staff for alcohol, tobacco, cocaine, and other drug use and who delivered between September 1, 1989, and August 31, 1991. Women of known human immunodeficiency virus-positive status were excluded ($n = 65$). The study design (requiring prospective pregnancy screening) also excluded women with no prenatal care. At follow-up, families were sought intensively by telephone, by mailing to the last known address, or, if lost to follow-up, by home visit. Client files of all Detroit-based university-affiliated hospitals and the pediatric, internal medicine, and ambulatory services were searched for updated contact information. In addition, children were sought through the private and public school systems. Additional information about pregnancy and the newborn period also was obtained from the perinatal database and newborn hospital charts. The final potential study sample consisted of 665 children and their families. Of the 665 families contacted, 94% agreed to testing. Exclusions included children who missed multiple test appointments, had major congenital malformations other than fetal alcohol syndrome (FAS), possessed an IQ of >2 standard deviations from the sample mean, and had incomplete data. In all, 506 parent-child dyads constituted the sample for this study.

Instruments and Procedure

At age 6 to 7 years, after informed consent was obtained, the child and the parent (biological mother when available or the primary caregiver) were tested in our research facility. Laboratory testing included the parent's self-reported psychopathology (Symptom Checklist-90¹⁰), parent-reported social support,¹¹ a modified Home Observation for Measurement of the Environment (HOME)¹² assessment, family socioeconomic status (SES) (A. B. Hollingshead, unpublished data), child IQ (Wechsler Preschool and Primary scale of Intelligence-Revised¹³), the child's self-report of exposure to violence,¹⁴ whole blood lead level, growth, the parent's report of child behavior (Achenbach Child Behavior Checklist [CBCL]¹⁵), and a structured interview to assess postnatal drug, alcohol, and cigarette use in the home. Research assistants who were trained and blinded to exposure status independently interviewed the child and caregiver.

Independent Variable

The independent variable in this study, prenatal alcohol exposure, was computed as the average absolute alcohol per day across pregnancy. At each prenatal visit, mothers were interviewed about alcohol use during the previous 2 weeks. Quantities and types of alcohol consumed were converted to fluid ounces of absolute alcohol and averaged across visits to generate a summary measure of alcohol exposure throughout pregnancy.¹⁶ Alcohol initially was used as a dichotomous variable comparing children who had had no prenatal alcohol exposure with children who had had any exposure. To evaluate the effects of different levels of exposure, we categorized the average absolute alcohol intake relatively arbitrarily into no, low (>0 but <0.3 fl oz of absolute alcohol/d), and moderate/heavy (≥ 0.3 fl oz of absolute alcohol/d) for the purpose of this study. There is no uniformly accepted definition of "low," "moderate," and "heavy" alcohol use during pregnancy in the literature.

Dependent Variable

The CBCL, a parent questionnaire that is applicable to children ages 4 to 16 years, is used widely in the clinical assessment of

children's behavior problems and has been used extensively in research.¹⁷ Designed at a fifth-grade reading level, it can be completed in 15 to 20 minutes and consists of 118 specific problem behaviors scored on a 3-category Likert scale. The test-retest reliability of the CBCL problem scores is high ($r = .89$).¹⁵ Achenbach derived 8 syndrome scales from the CBCL problem items by principal components/Varimax analyses.¹⁵ These are grouped further into Externalizing, or undercontrolled (Aggressive and Delinquent), behaviors and Internalizing, or overcontrolled (Anxious/Depressed, Somatic Complaints, and Withdrawn), behaviors. Three syndromes (Social, Thought, and Attention Problems) fit neither group (Neither Externalizing or Internalizing). A Total Problem score is computed by summing all problem items. Higher scores are associated with more problem behaviors. Raw scores are assigned T values, which provide a metric that is similar for all scales. Statistical analyses using T scores have less power because of data truncation but have the added dimension of distinguishing between scores in the normal compared with the clinical range. Achenbach proposed T scores of 60 and 67 as clinical cutoff points for the syndrome/total and problem subscales, respectively.¹⁵ Therefore, in this report, CBCL raw scores are used in *t* tests, analysis of variance, and regression analyses (as continuous data), and CBCL T scores are used for cross-tabulation and computation of odds ratio (OR; categorical data). Normative data for the CBCL were drawn from a national sample of 4- to 18-year-olds who had not received mental health services or special remedial classes within the preceding 12 months.¹⁵ Children who are below average in ability and achievement are likely to have higher scores on the Anxious/Depressed, Withdrawn, Aggressive, Delinquent, or Attention Problems scales.¹⁸

Control Variables

Data were collected on a broad range of control variables that are known to influence childhood behavior and/or to be associated with prenatal alcohol exposure. These included perinatal factors of maternal age; education; cigarette, cocaine, and other substances of abuse; and the gestational age of the infant. Postnatal factors studied included maternal psychopathology, continuing alcohol and drug use, family structure, SES, children's lead level, and exposure to violence.

Statistical Analyses

Statistical analyses were conducted using the SPSS statistical package (SPSS, Inc, Chicago, IL). Frequency distribution, cross-tabulation, and χ^2 tests were used for analyzing categorical data. The cross-tabulation table was used to examine relationships between categorical demographic variables and prenatal alcohol exposure groups using prenatal exposure as both a dichotomous and a categorical variable. The χ^2 test was used to test the association between prenatal alcohol exposure group and categorical demographic variables. Cross-tabulation with χ^2 test also was used to study the relation between dichotomous and categorical prenatal alcohol exposure and clinically abnormal CBCL T scores using the cut points recommended by Achenbach.¹⁵ OR was computed as the ratio of the odds of clinically abnormal scores for the group with prenatal alcohol exposure relative to the odds of clinically abnormal scores in the nonexposed group. Values of OR >1 indicate that clinically abnormal scores were observed with greater likelihood for subjects who had prenatal alcohol exposure than for those who had no such exposure. This would be evidence supporting that prenatal alcohol exposure promotes clinically abnormal CBCL scores. Ninety-five percent confidence intervals of the OR also were computed.

Continuous data were analyzed using *t* tests, analysis of variance with posthoc tests, and regression analysis. Independent-samples *t* test was used to define continuous demographic data and CBCL raw scores by dichotomous alcohol exposure. Analysis of variance was used to display continuous demographic data and CBCL raw scores by the ordinal prenatal alcohol exposure. The Scheffé posthoc test was used to determine which prenatal alcohol exposure group differed from the others. The Scheffé method is the most conservative of the available posthoc tests (false-positive rate is least). Stepwise regression was used to study the association between the independent (prenatal alcohol exposure) and control variables and the dependent variable (CBCL raw scores). The correlation coefficient (*R*) and adjusted r^2 were computed. The latter measure represents the proportion of variance of the dependent measure that can be predicted from the independent variable(s).

TABLE 1. Demographic Characteristics by Alcohol Exposure Group

Characteristic	Prenatal Alcohol			P Value
	No (<i>n</i> = 117)	Low (<i>n</i> = 323)	Moderate/Heavy (<i>n</i> = 66)	
Child				
Age	6.9	6.9	6.9	NS
Gender (% M)	49.6	51.7	53.0	NS
Birth weight	3124.0	3024.5	2699.8	.000
Gestational age	38.6	38.9	37.7	.002
Current lead ($\mu\text{g}/\text{dL}$)	4.8	4.7	6.0	.007
Performance IQ	85.5	85.2	85.0	NS
Mother				
Age	23.2	26.0	28.1	.000
Education	11.4	11.7	11.2	.030
Married (%)	32.8	27.0	21.5	NS
Cigarettes (number/d)	4.0	8.9	14.0	.000
Cocaine use (%)	18.8	45.2	69.7	.000
Current alcohol (oz AA/d)	0.04	0.4	0.5	.000
Current drugs (% use)	0.0	1.5	4.5	.061
Family				
Custody (biological mother)	87.2	85.4	62.1	.000
Custody changes (% yes)	16.5	21.1	35.4	.011
Father lives with child (%)	28.4	21.5	15.4	.108
Father drinks (%)	45.2	80.3	89.2	.000
Father uses drugs (%)	21.7	37.7	44.6	.002
SES	30.7	29.9	25.1	.001
HOME inventory	32.8	31.8	28.9	.012
Violence exposure	14.1	13.3	13.7	NS
Maternal depression	16.1	17.2	17.2	NS
SCL-GSI	0.5	0.5	0.5	NS

P values from corresponding *t* or χ^2 analyses. NS indicates not significant; AA, absolute alcohol; SCL-GSI, Symptom Checklist-Global Severity Index.

RESULTS

Almost one fourth of the women denied any alcohol exposure at conception and during pregnancy (25.4% and 23.2%, respectively). Periconceptionally, 26% of the women reported low alcohol use, and 48.5% reported moderate/heavy alcohol use. During pregnancy, however, the low alcohol exposure group represented 63.8% of the sample, and the moderate/heavy group accounted for 13%, suggesting that a significant number of moderate/heavy users of alcohol periconceptionally reduced their consumption during pregnancy. The mean of the absolute alcohol consumed per day among all women who reported alcohol exposure during pregnancy was 0.20 fl oz/d or equivalent to 3 drinks/wk. The maximum exposure, 5 fl oz/d, is equivalent to 10 drinks/d, or 70/wk. The mean consumption of absolute alcohol per day across pregnancy in the low prenatal alcohol exposure group was 0.08 fl oz, equivalent to having approximately 1 drink/wk. In the moderate/heavy exposure group, mean daily alcohol consumption was 0.79 fl oz, or 1.5 drinks/d across pregnancy.

Sample Characteristics

Six percent of the original cohort of 665 participants refused to participate in the evaluation at 6 to 7 years. An additional 40 dyads missed multiple testing appointments, and 28 had incomplete data for the variables of interest. Additional exclusions were the 4 children who had major congenital malformations. As mental retardation alone also can be associated with behavior problems, children with an IQ of >2 standard deviations from the sample mean were excluded. As a result, 47 children who had a performance IQ of <65 ($n = 31$) or for whom IQ testing was not available also were omitted from analyses presented in this article. Statistical analyses performed with and without these low-IQ children yielded similar results. In all, 506 parent-child dyads constituted the sample for this study. The mothers of subjects were significantly older and had more children than those who did not participate. However, the 2 groups of children did not differ significantly on any newborn characteristics, and mothers did not

TABLE 2. OR of Scoring in the Clinical Range by Dichotomous Alcohol Exposure

Parameter	OR	95% Confidence Interval	
		Lower	Upper
Externalizing	1.7	1.0	3.2
Aggression	1.3	0.7	2.4
Delinquent	3.2	1.3	7.6
Internalizing	1.6	0.9	3.1
Anxious/depressed	2.5	0.7	8.4
Somatic complaints	1.4	0.6	3.3
Withdrawn	1.4	0.5	3.4
Neither externalizing nor internalizing			
Social problems	1.3	0.6	2.8
Attention problems	1.1	0.6	2.1
Thought problems	0.9	0.5	1.9
Total score	1.8	1.0	3.0

TABLE 3. Mean CBCL Raw Scores by 3 Group Alcohol Exposure

Parameter	Prenatal Alcohol Exposure			P Value
	No	Low	Moderate/Heavy	
Externalizing	8.5	11.1	13.2	.002
Aggression	6.9	9.0	10.5	.003
Delinquent	1.5	2.1	2.7	.005
Internalizing	5.1	6.4	6.8	.105
Anxious/depressed	2.5	3.2	3.3	NS
Somatic complaints	1.1	1.2	1.5	NS
Withdrawn	1.7	2.2	2.1	NS
Neither externalizing nor internalizing				
Social problems	1.9	2.4	2.3	NS
Attention problems	3.2	3.7	4.4	NS
Thought problems	0.7	0.8	0.9	NS
Total score	23.7	29.0	32.2	.025

NS indicates not significant.

differ on prenatal use of cigarettes, alcohol, or cocaine.

Child

The mean age at assessment of the children in all exposure categories was 6.9 years. The proportion of girls and boys in all 3 groups also was comparable (Table 1). The mean gestational age and birth weights were progressively lower with increasing prenatal alcohol exposure ($P < .005$). The lead level was significantly higher in the group with moderate/heavy prenatal alcohol exposure ($P < .05$).

Maternal and Pregnancy

Maternal age at pregnancy was higher with increasing prenatal alcohol exposure, and maternal education was lower in the moderate/heavy exposure group ($P < .005$ and $.05$, respectively; Table 1). Marital status was comparable in the 3 alcohol exposure categories. Cigarette and cocaine exposure during pregnancy and current alcohol use were increased with increasing prenatal alcohol exposure ($P < .005$).

Family

Household composition was related to prenatal alcohol exposure (Table 1). Specifically, as prenatal alcohol exposure increased, the biological mother was less likely to be the primary caregiver ($P < .005$). There was a higher likelihood of child custody changes with increasing prenatal alcohol exposure ($P < .05$). Paternal drinking and drug use at the time of pregnancy also were highly correlated with prenatal alcohol exposure ($P < .005$), as were the family SES and HOME scores ($P < .005$ and $.05$, respectively). Maternal psychopathology and depression were comparable in the 3 prenatal alcohol exposure groups.

Child Behavior Outcome Using Alcohol as a Dichotomous Variable

The CBCL was available for 501 children. Univariate analyses of CBCL raw scores by dichotomous prenatal alcohol exposure groups revealed higher scores for the exposed children. The difference be-

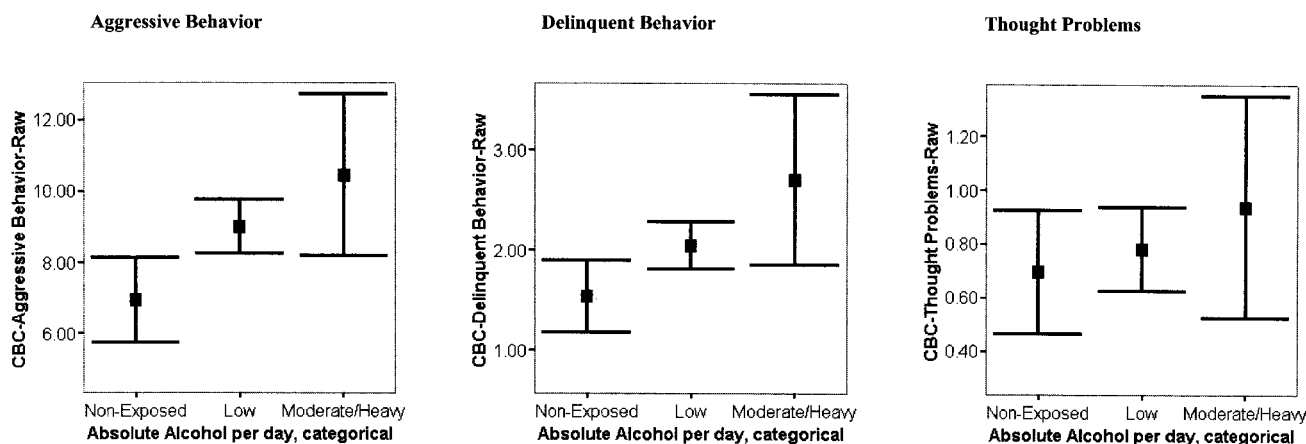


Fig 1. Error bar graphs show significant differences between no and low prenatal alcohol exposure for Aggressive behavior and between no and moderate/heavy group for Delinquent behavior. Between-group differences were not significant for Thought Problem scores.

TABLE 4. Percentage of CBCL T Scores Above Clinical Cutoff Points by 3 Group Alcohol Exposure Status

Parameter	Prenatal Alcohol Exposure			P Value
	No	Low	Moderate/Heavy	
Externalizing	14.8	22.5	29.7	.056
Aggression	11.3	12.3	21.9	.092
Delinquent	5.2	14.2	18.8	.014
Internalizing	11.3	17.2	17.2	NS
Anxious/depressed	2.7	6.6	4.8	NS
Somatic complaints	6.1	8.2	9.4	NS
Withdrawn	5.3	6.9	7.8	NS
Neither externalizing nor internalizing				
Social problems	7.9	10.7	7.8	NS
Attention problems	12.5	12.8	18.0	NS
Thought problems	9.6	9.4	9.4	NS
Total score	15.7	24.1	26.6	NS

NS indicates not significant.

tween the 2 groups was significant for Externalizing ($P = .002$; Aggression: $P = .002$; Delinquent: $P = .013$), Internalizing ($P = .038$; Anxious/Depressed: $P = .035$; Withdrawn: $P = .044$), and Total Problem scores ($P = .012$).

Clinically Abnormal Scores in Alcohol Exposed and Nonexposed Children

χ^2 analysis was performed using the cut points recommended by Achenbach for T score analysis¹⁵ on the CBCL. The OR (95% confidence intervals) of scoring in the clinical range in the exposed group was 3.2 (1.3–7.6) for Delinquent behavior, 1.8 (1.0–3.2) for Externalizing, and 1.7 (1.0–3.0) for Total Problem score (Table 2). These results suggest that children who are exposed prenatally to alcohol have significantly higher odds of having delinquent behavior.

Child Behavior Outcome Using Alcohol as an Ordinal Variable

Univariate analyses of CBCL behavior outcome by the 3 prenatal alcohol exposure groups revealed higher mean scores with increasing prenatal alcohol exposure for 9 of 11 subscales (Table 3). Significant

TABLE 5. Stepwise Regression Results for CBCL Scores Significantly Related to the Amount of Prenatal Alcohol Exposure

Parameter	Adjusted R ²	Standardized Coefficient β	P Value
Externalizing			
Maternal psychopathology	0.212	0.449	.000
Custody status	0.222	0.083	.050
Current lead	0.231	0.092	.028
Gender	0.238	-0.093	.026
Prenatal alcohol	0.255	0.139	.001
Aggression			
Maternal psychopathology	0.214	0.441	.000
Prenatal cigarettes	0.223	0.047	.290
HOME inventory	0.229	-0.097	.029
Maternal education	0.235	0.094	.030
Prenatal alcohol	0.248	0.128	.004
Delinquent			
Maternal psychopathology	0.130	0.352	.000
Custody status	0.155	0.143	.001
Current lead	0.166	0.110	.012
Gender	0.177	-0.113	.010
Prenatal alcohol	0.188	0.113	.011
Internalizing			
Maternal psychopathology	0.256	0.501	.000
Maternal education	0.265	0.093	.024
Prenatal alcohol	0.274	0.096	.020
Withdrawn			
Maternal psychopathology	0.168	0.416	.000
Custody status	0.180	0.093	.035
Current lead	0.188	-0.110	.011
Prenatal alcohol	0.198	0.110	.013
Attention problems			
Maternal psychopathology	0.169	0.387	.000
HOME inventory	0.184	-0.093	.014
Gender	0.193	-0.101	.020
Prenatal alcohol	0.199	0.093	.034
Total score			
Maternal psychopathology	0.291	0.537	.000
Custody status	0.297	0.064	.116
Prenatal alcohol	0.308	0.114	.005

between-group differences were observed for Externalizing (Delinquent and Aggressive) and Total Problem behaviors. Posthoc tests (Scheffé) revealed between-group differences to be significant for the no-exposure and low-exposure groups and the no-exposure and moderate/heavy-exposure group for Externalizing and Aggressive behavior. These findings suggest that for some behaviors (Aggressive), the adverse effects of prenatal alcohol exposure were evident even at low levels of exposure. For Delin-

quent and Total Problem behaviors, the difference was significant between the no-exposure and moderate/heavy-exposure group, suggesting a higher threshold for these behaviors. These results are illustrated in the error bar graphs in Fig 1.

Clinically Abnormal Scores and Alcohol as an Ordinal Variable

χ^2 test was performed using the cutoff scores recommended by Achenbach on the CBCL T scores. The percentage of children who scored in the clinical range on T scores was higher with increasing prenatal alcohol exposure for Delinquent behavior (Table 4). The OR (95% confidence intervals) for scoring in the clinical range for Delinquent behavior was 3.0 (1.3–7.3) for children with low levels of prenatal alcohol exposure compared with nonexposed children and 3.3 (1.3–8.7) for children with moderate/heavy prenatal alcohol exposure compared with nonexposed children.

Results of Stepwise Regression

Regression analysis was performed to determine whether prenatal alcohol exposure remained a significant predictor of childhood behavior after controlling for covariates and confounders (Table 5). Prenatal alcohol exposure across pregnancy was transformed to a log scale to normalize the distribution of the data and was entered into the regression model after all significant control variables. The control variables included birth weight, gender, gestational age, current age, and lead level of the child; prenatal exposure to cigarettes and cocaine; maternal age, education, marital status, and psychopathology; paternal drinking and use of drugs; and family composition, custody status, SES, HOME environment, and exposure to violence. Prenatal alcohol exposure remained a significant predictor of adverse behavioral outcome for Externalizing (Aggressive and Delinquent), Internalizing (Withdrawn), Attention Problems, and Total Problem Score. The amount of variance uniquely accounted for by prenatal alcohol exposure ranged between 0.6% and 1.7%. Maternal psychopathology was the most important predictor of behavior, accounting for 13.0% to 29.1% of unique variance in overall symptom scores. Gender also was a significant predictor: boys had higher scores on Externalizing (Delinquent) and Attention problems. Other factors that influenced childhood behavior included the child's custody status, current lead level, maternal smoking during pregnancy, maternal education, and the modified HOME inventory. Prenatal cocaine and current drug exposure did not enter the regression equation.

DISCUSSION

In this study of urban black children, low levels of prenatal alcohol exposure were associated with adverse behavioral outcomes on parent-reported child behavior. Higher mean scores on Externalizing and Aggressive behaviors were observed at low levels of prenatal alcohol exposure, whereas for Delinquent and Total Problem behaviors, higher mean scores were observed at moderate/heavy levels of expo-

sure. The OR of scoring in the clinical range for Delinquent behavior was 3.2 (1.3–7.6) in children who had had any prenatal exposure to alcohol compared with nonexposed control subjects. The relationship between prenatal alcohol exposure and adverse childhood behavior outcome persisted after controlling for other factors associated with adverse behavioral outcome in children.

Predicting the relation between prenatal alcohol exposure and child behavior is complicated by multiple prenatal, neonatal, and family factors as well as by the accuracy of the measure of exposure.^{19,20} Changing patterns of alcohol use in the general population over time also alter the generalizability of findings. It has been suggested that women underreport prenatal alcohol use when they are interviewed during pregnancy, compared with interviews conducted retrospectively after delivery.^{21,22} However, Jacobson's data from the Detroit study suggests that the detailed interview procedure during pregnancy, as was used in our study, provides a more accurate and reliable assessment of drinking during pregnancy than retrospective recall and the 1-time mid-pregnancy report used in previous studies.^{6,7,9,23}

In comparison to other studies,^{6–8,24–27} our results suggest that adverse effects of prenatal alcohol exposure are evident at much lower levels than previously reported. Driscoll et al²⁸ reviewed animal and human data and reported a dose-response continuum for neurobehavioral effects. Vorhees²⁹ suggested that neurobehavioral outcomes seem to be the most sensitive index of fetal toxicity. Although the adverse effects of moderate to heavy levels of prenatal alcohol exposure on childhood behavior have been documented extensively in the literature, there are limited data on the effects of low levels of exposure. Streissguth et al⁷ reported adverse neurobehavioral effects related to varying levels of prenatal alcohol exposure in the neonatal period, at 8 months, and at 4 years of age.⁷ Habituation, sucking pressure, and latency to suck were most affected on days 1 and 2. At 8 months, significant effects were observed on the Bayley Mental Development Index and Psychomotor Development Index scales; and at 4 years, reaction time, attention, and response latency were affected. Although laboratory tests could detect decrements in speed of information processing and sustained attention at much lower doses of prenatal alcohol exposure, clinically suspect or abnormal behaviors at 4 years of age were increased only at the heavier drinking levels (≥ 2 fl oz of absolute alcohol/d). Carmichael Olson et al²⁴ reported that even when the average alcohol intake remained within the parameters of social drinking (average consumption of a little less than 2 drinks per day of wine, beer, liquor, or combination), some children displayed significant deleterious learning and behavioral effects. These effects were demonstrated to persist with time, manifesting as antisocial behavior and substance abuse, school difficulties, self-reported intellectual and academic deficits, and laboratory observations of a negative presentation of self, impulsivity, and disorganization. Landesman-Dwyer and Ragozin⁶

reported that 4-year-old children whose mothers had drunk moderately during pregnancy (a mean of 0.45 fl oz absolute alcohol/d during pregnancy) had more maternal-reported evidence of hyperactivity or inattention compared with children whose mothers had drunk only occasionally or not at all during pregnancy. Streissguth et al²⁵ also reported deficits in attention at age 7 that were related to prenatal alcohol (mean absolute alcohol intake of 0.8 fl oz/d) in the form of continuous performance task errors of commission and delayed reaction time. In their comparison of children with FAS/fetal alcohol effects with children with attention-deficit disorder, Nanson and Hiscock²⁶ found that the attention deficits in the 2 groups were similar, although the children who had FAS/fetal alcohol effects were more intellectually impaired. In a prospective study of 103 black inner-city infants at a mean age of 6.5 months, Jacobson et al²⁷ demonstrated evidence of longer reaction times at lower levels of prenatal alcohol exposure (mean absolute alcohol intake of 0.5 fl oz/d) than those associated with FAS. Brown et al^{8,30} reported that children who were exposed to alcohol throughout pregnancy (mean absolute alcohol intake of 11.80 fl oz/wk) were more often described as showing externalizing behavior problems. The results of our study confirm findings at low levels of exposure with Externalizing (Aggression and Delinquent) behaviors most consistently affected. In contrast to the above reports, Coles et al³⁰ reported no differences in adaptive behavior among alcohol exposure groups (none, low, moderate). It is interesting that relatively low levels of maternal alcohol consumption (mean absolute alcohol intake of 0.42 fl oz/d) were related to decreased impulsivity both in the response inhibition task and by mother's perception of the child behavior at age 6 in the Ottawa Prenatal Prospective Study.³¹

The CBCL was the instrument used in this study to assess childhood behavior. Parents usually are the most knowledgeable about their child's behavior across time and situations.¹⁵ Parental involvement is required in the evaluation of most children, and parents' views of their children's behavior often are crucial in determining what will be done about the behavior. The CBCL has a screening sensitivity of 61%.³² In their 2-phase epidemiologic survey of 4- to 16-year-old Puerto Rican children, Bird et al³² reported that parent information was most informative in screening for childhood psychopathology. In the first stage of their study, the CBCL was used as a screening instrument; during the second stage, child psychiatrists evaluated children clinically. The authors suggested that parents who have known their children all of their lives would have precise information about their behavior. Similarly, Verhulst and van der Ende³³ reported substantial agreement between CBCL scores and clinical severity ratings of psychopathology by psychiatrists for 14-year-old children. Agreement was higher for Externalizing than for Internalizing behaviors. The correlation coefficient between the CBCL Total Problem score and their rating of the severity of problem behaviors was 0.63.

In the present study, the CBCL raw scores were used for the analysis of variance and regression analysis, whereas T scores were used for categorical analyses. The raw scores directly reflect differences between individuals without any truncation or transformation and hence have greater statistical power. Statistical analyses using T scores yield similar results as raw score analysis with less power and have the added ability of distinguishing between scores in the normal range compared with those in the clinical range. In this study, the CBCL detected significant differences in scores by prenatal alcohol exposure. Higher mean scores on Externalizing and Aggression were observed with low levels of prenatal alcohol exposure, whereas for Delinquent and Total Problem scores, higher mean scores were observed at moderate/heavy levels of prenatal alcohol exposure. Children who had had any prenatal alcohol exposure were 3.2 times as likely to have scores in the clinical range for Delinquent behavior. In Achenbach's sample, T scores of 67 and 60 significantly discriminated between referred and nonreferred children on the 8 problem subscales and syndrome/total scales scored from the CBCL, respectively. Reports in the literature suggest that these diagnostic thresholds of the CBCL may be too high.³⁴ Achenbach recommended that other cutoff points be chosen for particular research objectives and samples.¹⁵

It is not surprising that in the regression analysis, maternal psychopathology was the strongest predictor of childhood behavior. Jensen et al³⁵ reported that parental psychopathology is an important factor in predicting child symptomatology, accounting for 9.1% to 18.3% of the variance in overall symptom scores, with mothers' symptoms being the most salient. However, maternal psychopathology was not correlated with prenatal alcohol exposure in our study. Even after other well-known social/environmental variables were controlled for, the effects of alcohol exposure remain significant in predicting child behavior. The amount of variance that was uniquely accounted for by prenatal alcohol exposure in the present study ranged between 0.6% and 1.7%. However, it is important to recognize that although multiple regression seems to present an adjustment for bias, it lowers the estimated variance of a regression slope.³⁶ Thus, the variance in behavior scores accounted for by prenatal alcohol exposure probably is more than that reported in the regression model but less than that predicted by the unadjusted analysis. Likewise, Jacobson and Jacobson⁹ reported that for most measures of central nervous system function, moderate prenatal alcohol exposure explains 1% to 2% of the variance. As reported earlier, most common epidemiologic obstetric and perinatal risk factors were not independent predictors of behavior problems in children at 6 years.^{37,38} Child gender significantly affected behavior scores. Boys had more Externalizing (Delinquent) and Attention problems compared with girls. This is in agreement with the observations of O'Callaghan et al.³⁸ Other factors that were predictors of childhood behavior in the adjusted analysis were changes in the child's custody

status and higher child lead levels. Maternal/prenatal factors that were associated with problem child behavior included maternal smoking during pregnancy, lower maternal education, and lower scores on the modified HOME inventory.

Despite the important findings described in this study, there are potential deficiencies. Because women who reported high levels of drinking during pregnancy were oversampled, the prevalence of drinking during pregnancy in a randomly selected sample would be much lower. However, Sampson et al³⁶ reported that oversampling at high doses only increases the precision with which the dose-response relationship can be calibrated; it does not substantially alter the slope of the relationship per se. The women who enrolled in this study voluntarily sought prenatal care and were available for follow-up. Thus, the findings may not be generalizable to women whose alcohol and drug use interfered with access to prenatal care. Of the original cohort, 6% refused the evaluation at 6 years and an additional 6% missed multiple appointments and were not included. Although no differences at birth were detected between the children who participated and the group that refused additional study, it is possible that unmeasured differences exist between the sample studied and those who were lost to follow-up. However, no demographic data suggest that those who were lost to follow-up were in fact different from those who were tested. In longitudinal studies, subject losses over time because of inability to trace, migration, or refusal are inevitable.³⁹ The loss to follow-up may be of the magnitude of 20% to 30%.³⁹ An additional area of concern is that we reported the results only for children with an IQ of >65, as mental retardation alone may be associated with behavior problems. The likelihood of low IQ did not differ by exposure group, and in fact similar results were obtained when these cases were included in the analyses. The independent variable in this study was defined as the average absolute alcohol per day across pregnancy. Averaging alcohol exposure over all 3 trimesters could obscure the fact that there are important subgroups of women who are binge drinkers or who drink more heavily in 1 period of pregnancy than in the rest. An important aim of the analyses presented in this study was to demonstrate the adverse effects of low levels of alcohol exposure averaged across pregnancy on childhood behavior that have not previously been reported in the literature. The effects of pattern of prenatal alcohol consumption and timing of exposure are important and should be evaluated. Finally, although an extensive list of possible risk factors was considered in the regression analysis, it is possible that other unmeasured factors may account for the observed differences by alcohol exposure group.

CONCLUSIONS

Prenatal alcohol exposure was associated with adverse behavioral outcomes in children at age 6 in this large black, socially disadvantaged sample. The CBCL detected significant differences in scores by

prenatal alcohol exposure status. This effect was observed at average levels of exposure as low as 1 drink per week. Externalizing (Aggression and Delinquent) behaviors were most significantly affected. Higher mean scores on Externalizing and Aggression were observed with low levels of prenatal alcohol exposure, whereas on Delinquent and Total Problem behaviors, higher scores were observed only at moderate/heavy levels of prenatal alcohol exposure. Children who had had any prenatal alcohol exposure were 3.2 times as likely to have Delinquent behavior scores in the clinical range compared with nonexposed children. The relationship between prenatal alcohol exposure and adverse childhood behavior outcome persisted after controlling for other factors that are associated with adverse behavioral outcomes. The problems of children who are affected by even small amounts of parental alcohol use deserve recognition in clinical practice. Pregnant women should continue to be advised that there is no known "safe" amount of fetal alcohol exposure, and questions about prenatal exposure to alcohol should be routine in the psychological history for patients of all ages even in the absence of overt morphologic changes consistent with fetal alcohol exposure.

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**Prenatal Alcohol Exposure and Childhood Behavior at Age 6 to 7 Years: I.
Dose-Response Effect**

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