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Effects of Prenatal Alcohol Exposure at School Age. I. Physical and Cognitive Development[1]

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COLES, C. D., R. T. BROWN, I. E. SMITH, K. A. PLATZMAN, S. ERICKSON AND A. FALEK. *Effects of prenatal alcohol exposure at school age. I. Physical and cognitive development.* NEUROTOXICOL TERATOL **13**(4) 357–367, 1991.—Alcohol is a potent teratogen associated with dysmorphology, growth retardation, and neurological damage in children with the full fetal alcohol syndrome (FAS); alcohol is also associated with growth retardation and behavioral alterations in neonates prenatally exposed to various dosages. Questions remain about the long-term consequences of prenatal alcohol exposure. This study reports on the follow-up of a subsample of 68 children, the majority of whom were low income and black (mean age: 5 years, 10 months) who were first evaluated as neonates. Physical and cognitive outcomes of 25 children of women who drank throughout pregnancy [absolute alcohol (AA)/week: mean = 11.80 oz), even after receiving an educational intervention to stop drinking, were compared with outcomes of children in two contrast groups: a) women (n = 22) who stopped drinking (AA/week: mean = 11.46 oz) in the second trimester after an educational intervention but resumed postpartum; and b) women who did not drink during pregnancy and who drank little postnatally (n = 21). Children were compared for alcohol-related birth defects (ARBDs), growth (height, weight, and head circumference), and cognitive, academic, and adaptive measures. Neonatal and current physical measures were correlated to determine predictability of neonatal status. When the effects of age and gender were controlled, children in the continued-to-drink group showed significantly more ARBDs and had smaller head circumferences than those in the other two groups. When current drinking reported by caretakers was controlled, the children who were exposed throughout pregnancy also showed significant and consistent deficits in several areas of intellectual functioning including sequential processing (short-term memory and encoding) and overall mental processing. Alcohol-exposed children displayed significant deficits in preacademic skills when compared with children of nondrinkers, with both alcohol groups deficient in premath and reading skills. There were no differences in adaptive behavior at follow-up. These data suggest that alcohol exposure throughout pregnancy is correlated with persistent physical differences as well as identifiable deficits in sequential memory processes and specific academic skills. However, even when alcohol use is limited to the first part of pregnancy, significant deficits in academic skills and growth parameters are measurable.

Fetal alcohol syndrome (FAS) Prenatal alcohol exposure Alcohol-related birth defects (ARBD) Pregnancy Physical development Cognitive development

ALCOHOL is a teratogen that affects morphology and growth. It also affects behavior as a result of its actions on the developing central nervous system (15). The consequences for the human neonate have been studied extensively (4, 15, 36), as have outcomes in a number of children with the full fetal alcohol syndrome (FAS) (20,40). Nevertheless, many questions about the developmental consequences of alcohol exposure remain to be fully investigated. One issue is the extent to which the characteristic effects of alcohol exposure persist beyond infancy. Spohr, Willems-Bing and Steinhausen (34) have suggested that the physical stigmata associated with FAS become less apparent with maturity; other investigators have refuted this (37). Streissguth (37) has reported that, in FAS children, growth retardation is persistent, although weight tends to normalize, but in children who are mildly exposed, growth effects are not evident beyond infancy. Similar catch-up growth was reported by Ernhart and Kawano (10) in the Cleveland prospective study. However, Day et al. (8) report persistent, although not clinically significant, growth deficits in mildly exposed 3-year-old children from low-socioeconomic-status (SES) groups.

Finally, because of the potential interaction of development and postnatal rearing environment, the extent to which the cog-

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nitive impairments experienced by exposed children result from pre- versus postnatal factors is yet to be examined fully. It is this final area—cognitive development and behavior—that presents the greatest difficulty in assessment, although it is of considerable concern because of the potential implications for professionals dealing with the various consequences of alcohol exposure.

Some reports (11,12) suggest that, in the absence of physical dysmorphia, cognitive effects are not measurable, while other studies (39) find clear cognitive consequences of early exposure even in the absence of physical effects. In discussing behavioral teratogens, Vorhees (42) suggested a continuum of impairment in which neurological—hence, intellectual and behavioral—effects can occur even in the absence of obvious dysmorphology or abnormal growth rates. The alternative or threshold view is that, in the absence of physical markers, behavioral deficits are not present. According to this model, observed effects cannot be reliably assigned to the teratogenicity of alcohol but are assumed to be the result of environmental factors. This latter suggestion is difficult to refute without empirical evidence. The dilemma is to establish the etiology of these effects by separating the consequences of prenatal alcohol exposure from the background of clinical problems that often occur in the children of alcoholics. For instance, current drinking by caretakers as well as family dysfunction have been shown to influence cognitive development in addition to emotional and behavioral status (9). Of course, this concern is relevant also when children show growth retardation or dysmorphia, since women who abuse alcohol in pregnancy are likely to provide caretaking environments that are also affected by substance abuse.

When FAS was first described, retrospective research on developmental differences in the children of alcoholic mothers and clinically referred children identified as alcohol-affected was undertaken to identify persistent developmental effects. In most of these studies (20, 35, 40), dysmorphic children scored more poorly on tests of intelligence and motor and cognitive development and exhibited greater academic problems.

Although effects were less serious, a similar pattern of outcomes was noted in nondysmorphic children who were born to alcoholic mothers. Aronsson et al. (1) reported that alcoholics' children had significantly lower means on cognitive measures as well as a higher incidence of perceptual/motor problems than controls. Shaywitz et al. (27) reported behavior and learning problems as well as fine and gross motor difficulties in 15 children of normal intelligence born to alcoholic mothers. School failure, hyperactivity, and special educational referral also characterize such children.

Although suggestive, these studies were retrospective and correlational, making it difficult to respond to questions about environmental effects, selection bias, and other issues. For instance, many years later, the mother's pattern of prenatal alcohol use cannot be reliably established (24). A further bias is that retrospective studies typically overidentify problems associated with a particular cause (13). Therefore, as in investigations of other high-risk populations, prospective studies are more appropriate for exploring the teratogenic effects of substance abuse.

There are only a few longitudinal studies that prospectively follow alcohol-exposed children beyond infancy. In three samples (17, 26, 38, 39), there is evidence that prenatal exposure is associated with negative long-term outcomes other than physical effects in exposed children. Larsson et al. (17) reported that reduced drinking during pregnancy resulted in more positive outcomes at 2 years than continued drinking, although delays in speech development were evident in all alcohol-exposed children.

Streissguth et al. (38) reported on a sample of 4-year-old nondysmorphic children in a predominantly white, middle-class sample, finding that prenatal exposure to 1.5 ounces of AA per day (10.5 oz AA/week) was associated with a decrement in mean IQ scores of up to 5 points, even when potentially confounding factors, such as other prenatal drug use and parental education, were controlled. Similarly, at 7 years (39) in this same sample, what the authors referred to as "binge" drinking (>5 drinks per occasion) was associated with decrements in academic skills, memory, and attention. Language deficits and persistent differences in weight and height were not found in this sample. Russell et al. (26) have noted deficits in growth and in language development in children of heavy drinkers and those whose mothers could be described as "problem" drinkers during pregnancy. In the Cleveland prospective study, which involved a low SES sample (11,12), no developmental difficulties in cognition or language have been found to be associated with prenatal alcohol exposure. Thus, in addition to its sparseness, literature in this area has been inconsistent. The reasons for these inconsistencies are not completely clear, although, in the case of the Cleveland sample, it is possible that the high-risk conditions and low SES contributed to the floor effects which may have obscured results of alcohol exposure.

The study reported here is part of a longitudinal prospective research project on the effects of prenatal alcohol exposure in a low-income black population (4–6, 29–31). Neurobehavioral deficits in alcohol-exposed newborns were documented (5), as was persistence of these effects throughout the first month of life (6) and during later infancy (4). During infancy, the effects of prenatal exposure were most apparent in children who were exposed throughout pregnancy in contrast to children whose mothers stopped drinking in the second trimester (5, 30, 31). As in studies reported by Little et al. (18), Rosett et al. (25), and Larsson et al. (17), who also did a longitudinal follow-up, infants whose mothers stopped drinking after an educational intervention in the prenatal clinic demonstrated less serious outcomes, despite similar drinking levels during the early months of pregnancy (5,31) and despite their resumption of alcohol use postnatally.

In the present study, this "duration" distinction based on maternal behavior and infant exposure is maintained. Although it is evident that many of the deleterious effects on the infant result from exposure in the early part of pregnancy, continuing to use this discrimination appears to be meaningful because the factors making up this duration-of-exposure discrimination have been significantly, and repeatedly, related to infant outcome in this sample (4,5). Differences between the two groups of women who drank (stopped and continued) are detailed in our previous studies (4–6, 31). For this reason, in the current study, we hypothesized that continuing to drink alcohol throughout pregnancy would be associated with the highest risk for negative effects and that the most significant deficits would occur in the group of children so exposed. It was hypothesized that similar but less severe effects would be seen in the stopped-drinking group. If, when current alcohol use was controlled statistically, these two alcohol-exposure groups, which were similar on other factors, differed significantly on particular measures, these differences might provide some clue about specific deficits that may be due to third-trimester exposure. This effect—the duration of exposure, or third-trimester exposure—although strongly supported by animal models (43,44), has not been investigated in other human studies, with the exception of Larsson et al. (17). In animal models of the neurological effects of third-trimester exposure (43,44), specific effects were found in the hippocampus and the cerebellum, areas of the brain that are associated with learning and memory and with motor control, respectively.

The present study continued the follow-up of a subset of these children into the preschool and early school-age period.

TABLE 1

DEMOGRAPHIC CHARACTERISTICS OF MOTHERS AND CARETAKERS OF CHILDREN (MEAN AGE: 5 YEARS, 10 MONTHS) WITH DIFFERENT PRENATAL ALCOHOL EXPOSURE (N = 68)*

Maternal Characteristic	Prenatal Alcohol Exposure: Never Drank (n = 21)		Stopped Drinking (n = 22)		Continued to Drink (n = 25)		Statistics: F/χ^2	p
Mean age (years) (SD)								
Biological mothers	31.00	(4.58)	31.64	(5.48)	33.71	(5.01)		ns
Caretakers*†	same		same		36.50	(9.49)	4.37	<0.02
% Black	100.00%		86.4%		96.0%			ns
% Married*	23.8%		25.0%		17.49%			ns
Mean education (years) (SD)*‡	12.00	(1.22)	10.76	(1.70)	10.29	(2.59)	4.44	<0.02
Mean Slosson IQ (SD)*	75.24	(9.42)	75.73	(13.33)	73.04	(11.36)		ns
% Working regularly*								
Full or part time	75.7%		38.1%		47.8%		$\chi^2 = 21.27$	<0.006
Mean income per month ($)*	776.52	(783.18)	558.71	(503.85)	574.74	(387.38)		ns
Mean number of dependents*	2.50	(1.28)	3.05	(2.92)	2.96	(1.87)		ns

*At follow-up, 4 children were living with caretakers rather than biological mother: Grandmothers (3), foster parents (1). When marked (*) figures given refer to all caretakers, including natural mothers, so that children's environment can be described.

†Continued-to-drink group, includes 2 grandmothers, ages 61 and 63, significantly different from never-drank group and continued-to-drink group, which do not differ.

‡Never-drank group significantly different from stopped-drinking group and continued-to-drink group, which do not differ.

This longitudinal approach allowed examination of the effects both of prenatal exposure and of duration of exposure during gestation. In addition, because the majority of mothers who stopped drinking during pregnancy resumed in the postpartum period, this "stopped-drinking" group served as a contrast group providing an experimental control on environmental factors. Thus the design of this study, to some extent, provided a means to control for the effect of postnatal drinking through the inclusion of this group, which had a similar lifestyle and alcohol-use pattern to those in the continued-to-drink group. This kind of control is necessary because the findings that children reared in alcoholic families are affected by their parents' dysfunction (9) suggest that the effects of current drinking must be taken into consideration in interpretation of children's behavior.

METHOD

Subjects

Mothers and children were selected for the present longitudinal study from a larger cohort (N = 225) that participated in a study examining the effects on infants of alcohol exposure on newborns. Mothers and infants were recruited from 1980 through 1983. The original sample was drawn from women applying for prenatal care at a large university teaching hospital that serves a predominantly black, low-socioeconomic-status (SES) population. The subject pool included women who used alcohol and no other drugs, with the exception of cigarettes and, in some cases, marijuana, throughout pregnancy ("continued-to-drink"), despite an educational intervention during the second trimester. Also included were two contrast groups: a) women who drank an equivalent amount of absolute alcohol per week (AA/week) but who stopped by their second trimester after an educational intervention (31) ("stopped drinking": Discontinuation of drinking was established at a postpartum interview in the hospital and confirmed by family and/or medical professionals); and b) a randomly selected control group of non-alcohol-using mothers and their children from the same high-risk population ("never drank"). This abstinent group was used as the control group instead of women who used alcohol moderately because the majority of pregnant women (72%) in this low-SES, black population reported not drinking alcohol at the time that these data were collected. This group, therefore, served as the best representation of the population from which the sample is drawn.

During the postpartum period, medical records were reviewed, and infants were evaluated for medical, dysmorphic, and behavioral outcomes (5).

Because of limited resources and sample attrition, the entire sample could not be reassessed for this study. In selecting those to be included, subjects who had agreed to follow-up and who could be located by current address or phone number were identified from the data base. From this pool of potential subjects, a subsample of 5- to 8-year-old children from each exposure group was identified by birth date, and their mothers were recontacted. Subjects were telephoned, if possible; those who had no telephones were contacted by mail or in person. Those who agreed to participate were included in the study. The current study was explained, and informed consent for the follow-up procedures was obtained. Informed consent forms and study procedures were approved by the Emory University School of Medicine Institutional Review Board.

A total of 68 mother-child pairs were evaluated: "Never-drank" (21 nonexposed subjects), "stopped-drinking" (22 who were exposed through the second trimester of pregnancy), and "continued-to-drink" (25 who were exposed throughout pregnancy). At the time of this follow-up, four children from the continued-to-drink group were living with caretakers other than their biological mothers. Three children were in the care of grandmothers, and one had been adopted. Information about biological mothers (n = 64) and other current caretakers (n = 4) is presented in Table 1. This includes data on age, race, years of education, marital status, current monthly income, number of dependents, results of an aptitude test (IQ), and working status. Table 2 presents information about substance use by biological mothers during pregnancy and by current caretakers.

The neonatal characteristics of the children are shown in Table 3. Three preterm infants (<37 weeks gestational age) are included in the sample and are responsible for a statistically (but not clinically) significant difference in gestational age. These

TABLE 2

SUBSTANCE USE BY MOTHERS IN PREGNANCY AND MOTHERS/CARETAKERS OF CHILDREN (MEAN AGE: 5 YEARS, 10 MONTHS) WITH DIFFERENT ALCOHOL EXPOSURE DURING GESTATION (N = 68)*

Substance Abuse Variable	Prenatal Alcohol Exposure						Statistics	
	Never Drank (n = 21)		Stopped Drinking (n = 22)		Continued to Drink (n = 25)		F/χ^2	p
In Pregnancy								
Mean AA per week (oz.)†	0	(0)	11.46	(16.22)	11.82	(10.67)	7.76	0.001
"Binge" (>5 drinks per occasion)	0	(0)	3/22	(17%)	6/24	(25%)		ns
% Smoking cigarettes	19%		63.6%		95.8%		$\chi^2 = 27.89$	<0.0000
% Weekly marijuana use	1/21	(5%)	4/22	(18%)	5/25	(20%)		ns
At Current Assessment								
Mean AA per week (oz.) (SD) Mothers/caretakers‡	0.40	(0.80)	2.24	(2.76)	5.03	(8.95)	3.85	<0.03
Mean "Alcohol Severity" index (SD)†§	0.02	(0.04)	0.10	(0.13)	0.09	(0.10)	4.32	<0.02
Mean "Drug Abuse" index (SD)§	0.01	(0.01)	0.02	(0.06)	0.01	(0.03)		ns

*At follow-up, 4 children were living with caretakers rather than biological mother: Grandmothers (3), foster parent (1). When marked (*) figures given refer to current *caretakers* so their environment can be described.

†Never-drank group significantly different from stopped-drinking group and continued-to-drink group, which do not differ.

‡Never-drank group significantly different from continued-to-drink group.

§From Addiction Severity Index (21).

subjects were included at this follow-up because prematurity, in healthy infants, is not a factor in cognitive outcome by the age when testing was done.

To determine whether our sample was equivalent to the larger cohort from which it was drawn, we compared the group selected for our study with the subjects in the original cohort who were not included in the follow-up (n = 157) on a number of demographic variables considered potentially related to infant outcome. Of course, these were variables collected prenatally and in the neonatal period. Maternal variables were age, income, marital status, ethnic group, parity, use of marijuana, use of cigarettes, AA per week, and existence of maternal alcohol-related pathology (e.g., gastritis, liver damage). Infant variables were birthweight, head circumference, weight, gestational age, Apgar scores at 1 and 5 minutes, score on Obstetrical Complications Scale (19), and neonatal alcohol dysmorphia score (5,29). Two-way analysis-of-variance (alcohol-use group by selected/nonselected cohort) procedures indicated no differences on these measures due to selection/nonselection for the follow-up group. These findings suggest that the selected group was representative of the original cohort.

Procedure

After a home visit during which consent for follow-up testing was obtained and preliminary questionnaires were administered, mothers and children were transported to the Human Genetics Laboratory by project personnel; they were paid $20 for their participation. All testing of mothers and children was done individually by master's-level graduate students in psychol-

TABLE 3

NEONATAL CHARACTERISTICS OF CHILDREN WITH DIFFERENT ALCOHOL EXPOSURE DURING GESTATION (N = 68)

Infant Characteristic	Maternal Alcohol Use						Statistics	
	Never Drank (n = 21)		Stopped Drinking (n = 22)		Continued to Drink (n = 25)		F/χ^2	p
Mean gestational age (weeks)*	40.38	(0.97)	39.05	(1.94)	39.02	(2.50)	3.45	0.04
Mean birthweight (g)	3227.62	(347.55)	2947.95	(636.71)	2780.48	(788.99)	2.89	<0.06
Mean head circumference (cm)†	34.67	(1.20)	33.32	(2.00)	32.44	(2.45)	6.94	<0.002
Mean length (cm)‡	49.42	(2.23)	48.05	(3.65)	46.38	(3.65)	4.91	0.01
# Male	11/21	(52.4%)	9/22	(40.9%)	10/25	(40.0%)		ns
Mean Apgar (5 min)§	9.05	(0.22)	8.95	(0.59)	8.45	(1.01)	4.56	<0.01
Mean alcohol dysmorphia score (n = 54)¶	2.53	(2.98)	5.71	(6.44)	7.38	(9.06)	2.38	0.10
Mean obstetrical complications scale†#	110.29	(17.68)	91.52	(18.17)	86.17	(17.50)	10.94	<0.0001

*Never-drank group significantly different from stopped-drinking group.

†Never-drank group significantly different from stopped-drinking and continued-to-drink group, which do not differ.

‡Never-drank group significantly different from continued-to-drink group.

§Never-drank and stopped-drinking groups significantly differed from continued-to-drink group.

¶From checklist, Smith et al. (29).

#Littman and Parmalee; 1967 (18).

ogy who had professional training in psychological testing. Supervision was provided by the investigators. Mothers were interviewed using structured interviews and standardized tests. Testers who administered psychometric measures (e.g., Slosson IQ) were blind to mothers' group status. Testers administering measures related to substance use or psychiatric diagnoses, however, were necessarily familiar with maternal history. All examiners who tested children were blind to the mothers' prenatal and current drinking statuses and to the results of previous test batteries. None of the testers had previous involvement with this study or with the subjects. Blindness was more difficult to maintain with the few children who were obviously dysmorphic (n=4). The cognitive and physical measures, which took about 2½ hours to complete, were part of a longer battery, some of the results of which have been reported in Brown et al. (2).

Measures

Prenatal and neonatal descriptive statistics. Demographic and medical record information collected at the time of recruitment and at birth was reassessed to provide information about maternal demographics at the time of recruitment as well as substance-use history and infant neonatal growth data.

Maternal measures. Maternal measures were chosen to provide descriptive information and to identify current factors that might affect children's development. These included maternal demographic information, intellectual functioning, as measured by the Slosson Intelligence Test (28), and current alcohol and drug use and social functioning as measured by the Addiction Severity Index (ASI) (21), a measure that was not used at prenatal recruitment.

Children's measures. Measures were chosen to assess the areas of development that are characteristically affected by prenatal alcohol exposure. The domains measured were: a) physical status including alcohol-related dysmorphia and growth; b) cognitive development and academic functioning; and c) adaptive behavior.

Physical measures. Each child was given a physical examination by a master's-level pediatric nurse who was trained in the administration of the alcohol dysmorphia checklist (29) by the pediatric geneticist who had evaluated the children in the neonatal period. During this examination, the nurse assessed growth (head circumference, height, and weight) and general health and also examined the children for the presence of dysmorphic features associated with prenatal alcohol exposure. All evaluations were done without knowledge of the mother's drinking history or the child's medical or academic history.

Cognitive and intellectual functioning. The Kaufman Assessment Battery for Children (K-ABC) (16) is designed to measure a) the cognitive ability of children aged 2 to 12.5 years on the basis of processing style required for problem solving, and b) academic or preacademic achievement. The intelligence portion of the K-ABC rests on a convergence of several cognitive and neuropsychological theories that intelligence comprises two processes: one that is sequential, analytical, and temporal; and one that is holistic, gestalt, and spatial. The authors of the K-ABC identify these two cognitive processes as sequential and simultaneous, respectively. The Sequential and the Simultaneous Processing Scales represent two types of mental functioning that have been identified independently by Luria (20) and other researchers (7) on cerebral specialization. The K-ABC, whose subtests are similar to measures used by these neuropsychologists (7,20), has been used extensively both for clinical and for research purposes because of well-documented psychometric data (16). This test was chosen for use with this population because its subtests tap specific cognitive functions in which children with neurological impairment are likely to be deficient. Furthermore, it has specific norms not only for middle-class children but for low-income children. The administration time is approximately 45 minutes at the ages tested.

Adaptive behavior. The Vineland Adaptive Behavior Scales (32) assess personal and social capacities in communication, daily living skills, socialization, and motor skills. They are used to measure real-world coping skills versus cognitive and academic skills measured on tests of intelligence and achievement. Children's adaptive skills were measured for two reasons. First, in mildly affected children, deficits in daily behavior usually are not reported, so a measurement of this parameter was desired for comparison purposes. Second, like other measures of adaptive behavior, the Vineland was designed to tap different aspects of social competence than do aptitude and achievement tests. This instrument has excellent normative data as well as good reliability and validity. It is administered through a structured interview with the child's caretaker.

RESULTS

Analyses

Means or medians were computed for each of the measures in each of the domains studied. A series of multivariate analyses of variance, with and without covariates, was conducted to test the effects of maternal alcohol use on outcome. Related measures in different outcome domains (e.g., all K-ABC summary scores, all subtest scores, all Vineland scores) were analyzed in separate MANOVAs. In order to control for the effects of prenatal and current alcohol use, the amounts women reported drinking per week in ounces of absolute alcohol (AA/per week) at each time point (i.e., during the first part of pregnancy and at follow-up) were covaried in separate multivariate procedures (MANCOVAS). This allowed for the examination of outcomes as affected by reported maternal alcohol use at a given time while controlling for the effects of alcohol use at other time points. In addition, a MANCOVA for each outcome domain was conducted using as a covariate a measure of the severity of alcohol abuse as perceived by the respondent and the interviewer on the Addiction Severity Index (ASI), which was administered to all caretakers at the time of assessment of children.

These several analyses were necessary to test the hypothesis that the means for each of the drinking groups (never drank, stopped drinking by the second trimester, and continued to drink throughout pregnancy) were equal when current drinking was controlled statistically. Because of the small sample size, separate MANCOVAs were performed rather than including all variables in a single analysis. When multivariate analyses revealed significant effects, contrasts between the three groups of means were computed by Newman-Keuls post hoc analyses. When appropriate, covariance procedures were used to control the effects of potentially confounding variables. For instance, sex and age were used as covariates when current physical outcomes of children (e.g., height, weight) were examined, even though there were no significant differences between groups for these factors.

Physical Characteristics

Although the mean age for all children was 5 years 10 months, children's ages ranged from 5 years 3 months to 8 years 9 months, but did not differ significantly by group. Alcohol-related physical features (alcohol dysmorphia score) were assessed by using the checklist described by Smith et al. (29), based on the early work of Jones and Smith (15). These physical characteristics were consistent with those noted in the neonatal period

TABLE 4

PHYSICAL CHARACTERISTICS OF CHILDREN (MEAN AGE: 5 YEARS, 10 MONTHS) WITH DIFFERING PRENATAL ALCOHOL EXPOSURES (N = 68)*

	Maternal Alcohol Use in Pregnancy							
	Never Drank (n = 21)		Stopped Drinking (n = 22)		Continued to Drink (n = 25)		Statistics	
Physical Characteristic	M	SD	M	SD	M	SD	F	*p*
Age (years)	6.05	(0.43)	5.66	(0.72)	5.86	(0.95)		ns
Current weight (lb)	53.41	(7.94)	45.56	(9.12)	50.34	(13.39)		ns
Current height (in.)	47.76	(1.56)	45.82	(3.06)	45.87	(3.18)		ns
Current head circumference (cm)†	52.27	(1.29)	51.82	(1.49)	50.25	(3.85)	3.16	0.05
Alcohol dysmorphia score‡	2.20	(2.37)	3.95	(4.62)	6.75	(6.09)	5.22	0.008

*Multiple covariate analysis of variance procedure (MANCOVA), with sex and age as covariates, was used to analyze these figures. Reported statistical significance is for this procedure.

†Continued-to-drink group significantly different from stopped-drinking and never-drank groups, which do not differ.

‡Never-drank and continued-to-drink groups significantly different.

(see Tables 3 and 4). At follow-up, the never-drank and continued-to-drink groups differed significantly in the extent of physical effects noted, $F(2,65) = 5.22$, $p<0.008$.

There were more females than males in both alcohol groups (60% vs. 40%); the never-drank group had an even distribution. Since males are generally larger than females, gender was used as a covariate in comparing weight, height, and head circumference between alcohol-exposure groups. No effect of gender on these variables was indicated in this analysis. Since age varied over several years, this factor was also used as a covariate. A multivariate analysis procedure revealed a significant main effect, $F(6,110) = 3.40$, $p<0.004$. Height and weight approached significance; however, head circumference, $F(2,65) = 3.16$, $p<0.05$, yielded a significant effect (see Table 4). Results of Neuman-Keuls post hoc tests indicated that the continued-to-drink group differed from the never-drank group on this measure.

Correlations between physical characteristics and growth variables at birth and at follow-up indicated that alcohol dysmorphia scores and growth variables were significantly predictive in the alcohol-exposed children (dysmorphia score: $r = .80$, $p<0.000$; birthweight/weight: $r = .49$, $p<0.002$; length/height: $r = .43$, $p<0.009$; head circumference: $r = .46$, $p<0.004$). Only height and head circumference were predictive for the nonexposed group (length/height: $r = .57$, $p<0.04$; head circumference: $r = .55$, $p<0.04$).

Cognitive Measures

To examine the effects of maternal alcohol use on children's cognitive development, three sets of MANCOVA procedures were conducted on K-ABC data: a) summary scores (see Table 5), b) mental processing subtests, and c) academic subtests (see Table 6). Analyses using two of the covariates, AA/week during gestation and the current ASI (see Table 2), did not yield different outcomes than did analyses without covariates (which did, however, indicate significant differences among groups). However, when current drinking level (current AA/week) was covaried, the following results were obtained:

Summary scores. A significant main effect was found for this MANCOVA with current drinking level covaried, $F(10,114) = 1.89$, $p<0.05$, with significant univariate effects occurring for all of the summary scores, with the exception of simultaneous and nonverbal processing (both of which approached significance). These data are presented in Table 5. Newman-Keuls post hoc analyses indicated that the performance of the continued-to-

TABLE 5

SUMMARY OF STANDARD SCORES: COGNITIVE AND ACADEMIC FUNCTIONING ON K-ABC IN CHILDREN (MEAN AGE: 5 YEARS, 10 MONTHS) WITH DIFFERING PRENATAL ALCOHOL EXPOSURE (N = 68)*

	Maternal Alcohol Use in Pregnancy							
	Never Drank (n = 21)		Stopped Drinking (n = 22)		Continued to Drink (n = 25)		Statistics	
Subscale	M	SD	M	SD	M	SD	F	*p*
Sequential†	92.62	(15.43)	91.52	(10.73)	83.96	(12.48)	3.82	<0.03
Simultaneous	93.38	(11.66)	90.14	(12.77)	86.87	(13.67)		ns
Mental composite (IQ)†	91.91	(13.81)	89.29	(11.51)	83.91	(12.61)	3.15	<0.05
Achievement‡	94.65	(8.49)	87.95	(11.72)	85.65	(10.53)	6.47	<0.003
Nonverbal	91.43	(10.09)	89.76	(12.90)	84.95	(12.68)	2.49	0.09

*Multiple covariate analysis of variance procedure (MANCOVA), with current alcohol use in oz. (AA/week) as a covariate, was used to analyze these figures. Reported statistical significance is for this procedure.

†Continued-to-drink group significantly lower than never-drank and stopped-drinking groups.

‡Never-drank group significantly higher than stopped-drinking and continued-to-drink groups.

TABLE 6

SCORES ON K-ABC ACADEMIC SUBTESTS OF CHILDREN (MEAN AGE: 5 YEARS, 10 MONTHS) WITH DIFFERING PRENATAL ALCOHOL EXPOSURES (N = 68)*

	Maternal Alcohol Use in Pregnancy							
	Never Drank (n = 21)		Stopped Drinking (n = 22)		Continued to Drink (n = 25)		Statistics	
Subtest	M	SD	M	SD	M	SD	F	*p*
Faces/places	89.00	(12.68)	87.38	(12.29)	86.17	(11.49)		ns
Math†	96.52	(12.76)	86.67	(14.85)	84.83	(13.31)	5.64	<0.006
Riddles	93.00	(9.28)	89.52	(9.63)	89.65	(10.18)		ns
Reading/decoding‡ (n = 59)	101.76	(12.38)	99.12	(9.56)	91.62	(15.63)	3.98	<0.03

*For 1st 3 subtests, analysis used MANCOVA procedure with current oz. (AA/week) as covariate. For "Reading," which has different n, ANCOVA procedure was used. Statistical significance is based on these procedures.

†Never-drank group significantly different from stopped-drinking and continued-to-drink groups, which do not differ.

‡Never-drank group significantly different from continued-to-drink group.

drink group was significantly different from both the stopped-drinking and the never-drank groups for the sequential processing and mental composite (IQ) scores. However, the achievement summary score of the never-drank group is significantly higher than the scores of both alcohol groups. These data indicate that, when confounding effects of current drinking are controlled, effects of prenatal exposure are apparent. The same pattern of outcomes was obtained using a multivariate procedure without covariates, although significance levels were slightly lower. Thus the observed effects appear to be attributable more to prenatal

TABLE 7

CHARACTERISTICS OF "DYSMORPHIC"* CHILDREN AND THEIR MOTHERS/CARETAKERS (n = 8)

	Children's Case Number							
	109†	112	159	190	273	293	322	359†
Duration of alcohol use in pregnancy	cont.	cont.	stop	stop	cont.	cont.	stop	cont.
Reported maternal AA per week/oz. in preg.	2.00	10.00	16.00	4.00	6.00	1.00‡	34.00	21.00
"Binge" (>5 dK/Occ)	no	yes	no	no	yes	no	yes	yes
Maternal IQ (Slosson at follow-up)	59	68	76	54	71	¶	66	59
Race	B	B	B	B	B	B	B	B
OCS§	80	—	81	121	60	81	57	87
Current caretaker's AA use (oz. per week)	1.57	5.00	6.00	3.00	17.50	0.38¶	2.02	0.00¶
Current ASI severity	0.02	0.11	0.03	0.03	0.18	0.05¶	0.08	0.00¶
Neonatal								
Sex	F	M	F	M	M	M	M	F
Gestational age (weeks)	41	39.5	38	40	39	39	38	33
Birthweight (g)	2190	2160	2410	3230	2400	1840	2140	1040
Head circum. (cm)	32	30.5	33	35	31	30	32	27
Length (cm)	45	43	47	48	43	44	46	36
Alcohol dysmorphia score	19	24 (2 years)	15	—	29	17	25	29
Current								
Age	6.9	7.6	6.1	5.5	5.6	6.9	5.5	5.4
Weight (lb)	39.50	40.50	43.25	34.50	34.00	33.75	28.00	29.00
Head circum. (cm)	48.8	44.0	53.5	52.5	48.0	48.5	48.0	44.0
Height (in.)	46.75	46.75	45.25	41.25	40.50	41.50	40.00	42.00
Alcohol dysmorphia score	14	21	4	12	14	10	17	22
K-ABC mental	89	50	98	107	91	80	68	70
Vineland ABC	103	63	112	98	95	80	97	78

*Dysmorphic = score on alcohol dysmorphia scale ≥15; 20 = FAS (27).

†Cases 109 and 359 are sisters.

‡Reported drinking one-fifth of whiskey a day prior to pregnancy.

§Obstetrical complications scale (19).

¶Nonmaternal caretaker.

exposure than to current maternal alcohol use.

Individual cognitive subtests from the K-ABC were analyzed in a similar fashion. MANCOVA analyses did not yield a significant overall effect for this group of variables. However, to determine the locus of the significant difference in the sequential processing summary score, these subtests were analyzed using univariate analyses. Only on hand movements, a visual sequential test of short-term memory and sustained attention, did the one-way analysis of variance show a significant difference: The continued-to-drink group performed more poorly, $F(2,65) = 4.23$, $p<0.02$, than the never-drank and the stopped-drinking groups, which did not differ. However, on all but one subtest, the continued-to-drink group performed less well than the other groups. These findings may indicate that statistical power was insufficient to identify subtle differences.

The achievement subtests from the K-ABC are shown in Table 6. A MANCOVA involving the first three subtests, faces/places, math, and riddles, with current maternal drinking used as a covariate, yielded a significant effect, $F(6,118) = 2.35$, $p<0.04$. Subsequent univariate analyses yielded significant effects for the math subtest, which involves early math skills, with the never-drank group scoring significantly higher than both the stopped-drinking and the continued-to-drink groups, which did not differ. The reading/decoding subtest, which has a smaller "n" due to age and ability differences in children, was analyzed in an analogous manner to the first three subtests using an analysis of variance with covariate (ANCOVA) procedure. On reading/decoding, which involves identification of letters and words, the never-drank group scored significantly higher than the continued-to-drink group.

Adaptive Behavior

Using the multivariate procedure, with current maternal drinking as the covariate, no significant differences were found in scores on the Vineland Adaptive Behavior Scale, indicating that maternal alcohol use and prenatal alcohol exposure were not related to mothers' reports of children's adaptive functioning. All scores were within the average range.

Threshold Versus Continuum

In this sample, eight children (three from the stopped-drinking group, five from the continued-drinking group) had scores on the newborn Alcohol Dysmorphia Checklist (29) greater than 15, which is the cutoff score we defined as indicating the physical effects of alcohol, often called alcohol-related birth defects (ARBDs), or fetal alcohol effects (FAEs). Up to 9 points of this total score could result from growth factors (e.g., birthweight, head circumference). However, to achieve a score of 15, a child would have to exhibit some of the facial features associated with alcohol as well as the growth effects. To ensure that the cognitive effects obtained in this study were not simply the result of deficits in this group which shows the most severe physical effects, we removed these children from the sample and repeated all analyses. Probably because growth was included in the dysmorphia score, exclusion of these children eliminated growth differences between the exposure groups when age and sex were controlled. For the cognitive measures, scores in both the stopped-drinking and the continued-to-drink groups were changed slightly, usually higher by 1 or 2 points. However, the pattern of results did not change at all, and significant differences persisted in achievement, math, and reading scores. On some factors (i.e, Apgar scores, Vineland motor, maternal age), elimination of this group of children led to a greater discrepancy between the alcohol groups and the nondrinkers than was shown previously. This outcome suggests that the alcohol effects on the variables collected, and on these cognitive skills in particular, could most reasonably be viewed as a continuum. Because this finding suggests that it is not appropriate to omit this group of children, we have reported the results for the whole group. We have presented some data regarding these children in Table 7. Examination of this table indicates the wide range of outcomes exhibited by these children.

DISCUSSION

This follow-up study was undertaken to investigate the effects of maternal drinking on children's developmental outcomes in a sample drawn from a predominantly black, low-SES population. Of interest was the extent to which the teratogenic effects of alcohol, usually observed in the newborn, persisted over time in a sample of children with a wide range of prenatal exposure. In addition, the present study allowed some control over postnatal environmental effects in two ways: First, by inclusion of the stopped-drinking group, which was similar to the continued-drinking group, and second, by statistically controlling for the effects of current drinking by biological mothers and caretakers.

To examine developmental outcome, we evaluated the areas that are used to define prenatal alcohol effects—dysmorphia, growth, and signs of neurological deficits, particularly cognitive effects—in children (mean age: 5 years 10 months) who had been exposed to different durations of prenatal alcohol exposure: "never drank" (children whose mothers were abstainers); "stopped drinking" (children exposed until the second trimester, when the mothers stopped after an educational intervention); and "continued to drink" (children exposed throughout pregnancy despite a similar intervention at the time of recruitment). In addition, we separately covaried all outcome measures using two measures of postnatal alcohol use: a) current alcohol use as measured by absolute alcohol per week using a quantity/frequency measure (3), and b) an "alcohol severity" index, which is derived from information given on the ASI (21) and which included self-reported indicators of alcohol use, as well as perceptions of respondent and interviewer about the severity of the alcohol-use problem shown by the respondent. Examination of Table 2 indicates that the alcohol groups do not differ significantly from each other on these variables, although the nondrinking group is significantly different.

Physical Effects

Within the alcohol-exposed group, stigmata specific to alcohol exposure (i.e., facial features) persist over time and seem to be evident to trained personnel at follow-up. There is a high correlation ($r = .77$, $p<0.0001$) between ratings of severity of dysmorphic effects at 3 days and at the current assessment point (29), although there is some diminution of the severity of the weight discrepancy in many of the alcohol-exposed children, which may have affected dysmorphia scores somewhat. In a similar way, reductions in head circumference in children who have been exposed to alcohol appears to be persistent over time. Although alcohol dysmorphia ratings were not as high at 6 years as at 3 days in some children (see Table 7), evidence for the effects of alcohol exposure was clearly present, and these findings seem to be consistent with Russell et al. (26) and Day et al. (8), who found that dysmorphic features and/or growth effects were persistent. It is probable that these findings and those of Spohr and Steinhauser (33,34) are not really discrepant. There may be a number of reasons for the apparent differences in outcome. For instance, ratings of dysmorphia may differ with the sample used, the amount of exposure, the form of dysmorphia

checklist used, or other methodological factors. Like the outcomes in our study when the dysmorphic children are removed, Streissguth et al. (38,39) did not show persistent growth deficits relative to controls in middle-class non-FAS children.

Cognitive and Behavioral Effects

Cognitive scores on the K-ABC are generally lower for the two alcohol-exposed groups; the group whose mothers reported continuing to drink has the lowest scores on all but one of the subtests. These scores are significantly lower in sequential processing, achievement and the mental processing composite (which is referred to as equivalent to an IQ score on other standardized measures of intelligence), particularly when effects of current drinking are controlled. These patterns indicate a generalized effect but also suggest that there may be specific cognitive functions more vulnerable to damage due to prenatal alcohol exposure. More specific neuropsychological and educational evaluation of these functions will be required to provide a more specific understanding of these deficits, the brain structures underlying them, and their implications for learning and remediation.

In this sample, sequential processing skills seem more affected by continued exposure to alcohol than are simultaneous processing skills, for which differences did not achieve significance. On the sequential subtests as well as the summary score, the children whose mothers stopped drinking did not perform differently from the children of the never-drank group. The subtests that make up the sequential score are: a) hand movement, which involves short-term memory for visually presented, novel stimuli; b) number recall, a test of short-term recall of auditorially presented numbers similar to the digit span subtest of the Weschler scales; and c) word order, which involves short-term memory for auditorially presented words, as well as perceptual/motor coordination.

Short-term memory processing, often called encoding, is believed to be mediated by subcortical structures, including the hippocampus (23), which are particularly susceptible to the effects of alcohol. In adults, alcoholism can result in deficits in these encoding processes, the most severe of which is Korsakoff's Syndrome (23). Autopsy studies of Korsakoff patients have found lesions in this midbrain region (41), and it is also this area of the brain that West and his colleagues (43,44) found to be affected by the equivalent of third-trimester alcohol exposure in animals. Taken together, these reports suggest that third-trimester exposure may affect the developing hippocampus or allied structures, leading to deficits in the ability to encode visual or auditory information. Alternatively, since it is clear that exposure early in pregnancy has serious consequences for the developing fetus, stopping drinking may permit the fetus to achieve some "recovery" in this area of cognitive development, as in birthweight and other areas of growth (e.g., head circumference, length).

Although this explanation of the reported results appears plausible, it is important to regard such speculation with caution. Many alternative explanations for the present findings could be generated. It may be that mothers who discontinued drinking during pregnancy consumed less alcohol during the first two trimesters, so observed effects are the result of this lower "dose" of alcohol rather than of exposure during a specific time period. However, both the measures of amount/frequency (AA/week) and the frequency of "binge" drinking as reported by mothers (see Table 2) argue against this explanation, since groups are not significantly different on these factors. Another possibility may be that other unmeasured differences among these groups of women affect children's outcomes (31).

The results of the achievement portion of the K-ABC battery may be useful in identifying the kinds of problems considered a result of prenatal alcohol exposure. Math skills and prereading identification of words and letters are significantly lower in both alcohol groups. These findings suggest that alcohol-exposed children are likely to experience academic difficulties, and it is possible that some of these children will develop specific learning disabilities. The extent and the nature of these difficulties warrant further investigation, including a more detailed assessment of their academic skills and their progression through school.

These findings are in contrast to those on the Vineland Scales, which evaluate everyday coping skills. At this follow-up, adaptive behaviors were not significantly affected by the results of prenatal alcohol exposure or postnatal maternal alcohol use. Since potential problems in encoding and academic skills are not evident in daily functioning, affected children may go undetected until problems arise in the academic environment.

Although suggestive, this study has limitations. The first is sample size. Because limited resources allowed only a subsample of children to be retested, we could not control statistically for the effects of some potentially confounding variables, such as cigarette use and other lifestyle variables. Thus some effects attributed to maternal alcohol use may, in fact, be the result of factors associated with maternal drinking or with unassessed differences among these groups of women. Although current drinking level and severity of alcohol use were controlled statistically, other factors in the postnatal rearing environment, such as maternal education, were not considered in this study. Although it may be impossible to control all potentially confounding factors, the addition of more subjects would allow for an examination of the effects of other family variables and emotional/social functioning on the child's outcome. Such a study is currently under way in our laboratory with a group of older children. However, it is not always appropriate to attempt to control all factors statistically. In this study, to the extent possible, the variability associated with other confounding factors (e.g., race, other drug use pre- and postnatally, SES, hospital of birth, parity, etc.) was controlled by means of the experimental design.

Another limitation is that some of the factors of potential interest (e.g., current paternal factors, environmental precursors of current behavior) could not be assessed when children were retested for this study because of practical problems. Finally, it is important to remember that much of these data are based on maternal self-report, with all of the limitations that such data imply. Continuing to drink, for instance, may be associated with less accurate reporting of both substance use and information regarding children's competency.

Despite these real limitations, the theoretically consistent and specific differences seen in the alcohol-exposed children suggest that these differences may be real effects of prenatal exposure. In addition, convergent data from several similar studies suggest that growth and cognitive outcomes may be similar in different populations (26, 36, 39).

In summary, in this low-income, black sample, the physical effects of prenatal exposure seem persistent, and the early identification of affected children appears possible. In addition, there are certain specific cognitive consequences when current drinking is controlled for, and duration of exposure may be related to particular cognitive and physical outcomes. With longer alcohol exposure prenatally, there is a generalized lowering of cognitive scores, and exposure throughout pregnancy seems related to deficits in encoding, particularly the processing of visually and auditorially presented lists into short-term memory. In addition, for both groups of alcohol-exposed children, deficits were noted in math skills and prereading skills.

We do not suggest that prenatal alcohol exposure is the only

cause of such deficits or that potential deficits associated with alcohol use are confined to such functions or areas. More refined neuropsychological assessment might reveal other areas of strength and weakness. However, these data provide a beginning in the more focused examination of the long-term effects of prenatal exposure and may guide research on the educational remediation of affected children.

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