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Early Identification of Risk for Effects of Prenatal Alcohol Exposure*

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ABSTRACT. *Objective:* Fetal alcohol syndrome (FAS) and less severe outcomes are typically diagnosed later in childhood, although earlier diagnosis of the effects of exposure would allow intervention in infancy and prevention of associated secondary disabilities. Identification is particularly difficult in such high-risk groups as low-birthweight infants. The goal of this study was to develop methods for early identification of at-risk infants. *Method:* Three methods (microcephaly, heavy episodic drinking [≥ 5 drinks/occasion] in pregnancy and a cumulative risk index) identified neonates at risk for those developmental consequences of prenatal exposure that can be measured at 6 and 12 months (i.e., standard scores on Bayley Scales of Infant Development and growth measures). The usefulness of these methods was assessed by comparing those infants selected to an unexposed contrast group, while controlling for potentially confounding factors (e.g., race, socioeconomic status and birthweight). *Results:* At 6 months, when 70 infants were tested, trends were found for lower language facet scores and lower scores on the Behavioral Regulation Scale; at 12 months, when 134 were tested, alcohol-exposed infants had significantly lower cognitive facet scores ($p < .02$) and were more likely to be classified as either mildly or significantly developmentally delayed ($p < .02$). *Conclusions:* It is possible to identify infants at risk for alcohol-related developmental delays using information available in the neonatal period, although it is not usually done. Of the three methods tested, a cumulative risk index based on maternal characteristics was found to be most predictive. (*J. Stud. Alcohol* **61:** 607-616, 2000)

EARLY IDENTIFICATION of alcohol-affected infants, both those with fetal alcohol syndrome (FAS) and those less obviously affected, could provide the opportunity for significantly improved services for both mothers and infants. Identification in infancy would permit early intervention with affected children and their families (Stratton et al., 1996) and limit many of the negative behavioral and emotional conditions associated with FAS (Streissguth et al., 1996). In addition, early identification would provide an opportunity for intervention with, and treatment for, alcohol-abusing women that might improve their prognoses as well as limit the number of subsequent FAS births. Early identification would also allow improved surveillance and more effective planning for, and monitoring of, public health policy.

Although important, identification of FAS and other effects are difficult because of limitations in the application of the diagnostic criteria during the neonatal period. These diagnostic criteria include characteristic facial features, growth retardation and evidence of neurodevelopmental deficits (Jones and Smith, 1973; Sokol and Clarren, 1989; Stratton et al., 1996). However, it can be difficult to discriminate the facial features associated with FAS in newborns (Aase, 1994; Abel et al., 1993; Clarren et al., 1987; Ernhart et al., 1995), and growth deficits, while associated with alcohol exposure, are not specific to that disorder (Jones, 1988). Finally, neurodevelopmental outcomes are not easily measured during early infancy (Coles, 1996). Although the newborn nursery would be the most logical and efficient location to focus a screening process, without reliable biological markers individualized assessments on every infant born is costly and inefficient (Stoler and Holmes, 1999). As a consequence, other kinds of markers for identifying at-risk infants are needed. In order to be useful in screening, such information must be: (1) collectible in the neonatal period; (2) associated with maternal alcohol abuse during gestation; and (3) related to developmental outcome.

Low birthweight as a marker. Birthweight is easy to ascertain and because prenatal alcohol exposure is associated with intrauterine growth retardation (IUGR; Abel, 1998), low(er) birthweight might be used to select neonates in need of additional assessment. However, growth retardation is not specific to FAS (Jones, 1988) and selecting all children who are small for gestational age (SGA) would not be cost effective for broad scale follow-up. Additional criteria are needed to reduce numbers further and target those children most at risk for the neurodevelopmental compromise associated with the cognitive and emotional deficits that are most significant for later functioning.

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For such identification, direct behavioral assessment of neonates is not sufficiently sensitive and specific. In addition, such tests are expensive and time consuming and do not correlate highly with later measures of functioning (Bornstein and Krasnegor, 1989). Therefore, it may be more productive to concentrate on other kinds of predictors. While a variety of measures can differentiate alcohol-exposed from other infants at birth, the more important questions are whether such discriminations have long-term validity and whether the additional information will add to the risk associated with being born growth retarded.

Previous research suggests several strategies for identifying predictor variables that are of potential importance in identifying children at risk for FAS or alcohol-related neurological damage. These include some characteristics of infants (Coles, 1996; Jones and Smith, 1973) and some of mothers (Bresnahan et al., 1992; Day et al., 1993; Jacobson et al., 1996). In addition, based on work with other kinds of high-risk groups, the possibility of developing a cumulative risk index (CRI) for prediction should be considered (Field et al., 1978). To examine the relative merits of such information, we selected three methods that could be implemented using information obtainable in the neonatal period and then evaluated them by following two subsamples of identified infants during the first year to test neurodevelopmental status and growth. The three methods (discussed in operational terms in the Method section) were: (1) disproportionately small head size at birth (microcephaly); (2) maternal report of episodic heavy drinking (≥ 5 drinks/occasion); and (3) scores on a cumulative risk index based on maternal characteristics. As it was important to discriminate effects of growth retardation per se from those associated with the alcohol-related effects, contrast groups were selected from nonexposed infants who had similar birthweights and demographic characteristics. It was hypothesized that these methods would identify alcohol-exposed children who could be discriminated from controls in terms of their neurodevelopmental outcomes, and that the results would, therefore, contribute to the development of future screening programs.

Method

Subjects

Surveillance sample. Participants in the current study were a subsample of a larger surveillance study of the relationship between low birthweight and alcohol exposure (Drews et al.,1999, unpublished). In that study, all births in two hospitals, the first serving an inner city, low socioeconomic status (SES) population and the second, a suburban middle-class population in the Atlanta metropolitan area, were screened and 1,009 infants recruited from the following birthweight categories: (1) <5th percentile (small for gestational age, or SGA); (2) 5th to 10th percentile; (3) 11th to 95th percentile (average for gestational age, or AGA); and (4) >95th percentile (large for gestational age, or LGA). Low birthweight infants were oversampled; 65% of the sample could be described as growth retarded (categories 1 and 2) relative to the norms used (Yips, 1993). Medical records regarding the pregnancy and delivery were abstracted and mothers of identified infants participated in a structured interview assessing demographic information, drinking habits, other drug use, pregnancy information, general health and food intake.

The "at risk" sample for follow-up. To identify infants at risk for later neurodevelopmental problems associated with prenatal alcohol exposure, three criteria were used, with the intention of comparing their usefulness in predicting outcomes:

1. *Disproportionate head circumference (HC).* Because it is part of the defining criteria for FAS (Sokol and Clarren, 1989) and is also associated with developmental delays (Jones, 1988), microcephaly is a potentially useful marker. In addition, HC is a relatively reliable measurement, one routinely obtained in the newborn period in all medical settings. However, simply selecting for reduced head size relative to population norms is not a reasonable strategy in sampling from a group of SGA infants since most will have a smaller HC than "average" infants. Instead, identifying children whose HC is small relative to body mass may more appropriately flag those with neurodevelopmental compromise.

Body mass was operationalized as ponderal index (PI), based on a body length/weight relationship (Miller and Hassanein, 1971). To define a cutoff score for selection, a regression formula was used to predict head size for PI within each of the hospital sites used in the surveillance study. The formulas were: Expected $HC = B_0 + (PI^*|B_1|)$; Difference in HC = (Actual HC-Expected HC/[Mean of Residuals]). Children whose HC's were in the lower 5th percentile of the studentized residuals of predicted HC for PI were selected for follow-up.

2. *Heavy episodic drinking.* This criterion was operationalized as a maternal report of five or more drinks per occasion at any time during pregnancy. In a number of studies (Abel, 1998; Streissguth et al., 1994), maternal self-report of heavy episodic drinking, as defined here, is highly correlated with cognitive and behavioral deficits in offspring. In addition, such drinking patterns are not uncommon among pregnant women in both lower and middle class samples and may be increasing (Ebrahim et al., 1999). Using heavy episodic drinking as a selection criterion has the advantages of simplicity and support from previous work. There may be some limitations in generalization of this criterion, as self-report of alcohol consumption during pregnancy may result in a sampling bias from different SES groups (Day et al., 1993). It is also likely that those who drink more heavily also drink more frequently.

3. *Cumulative risk index (CRI).* Because the nature of early development precludes direct assessment of neurocognitive status, cumulative risk indices often are most useful in

identifying cognitive risk in young infants (Field et al., 1978). For this study, a Maternal Substance Abuse (MSA) Checklist, a 17-item scale, was designed to integrate maternal report of alcohol consumption prior to and during pregnancy with various other indices and correlates of alcohol abuse that are available in medical records (see the Appendix).

Elevated MSA Checklist scores were associated with lower birthweight, smaller head circumference and shorter body lengths in the neonatal period (Coles et al., unpublished manuscript, 1999). One advantage this method has over maternal report of heavy drinking is the identification of women across all social classes. A limitation is the need to collect information from maternal report and medical records to complete the checklist. For this study, the selection criteria used a cutoff score of ≥ 7 (of 17) items.

Selection of "at risk" and control groups. Most infants in this study could be considered "at risk" due to lower than average birthweights. Therefore, to distinguish effects associated with IUGR from those associated with the alcohol-related criteria, it was necessary to control this factor. Based on MSA Checklist score, heavy episodic drinking and/or head size, 163 potentially alcohol-affected infants were identified in the Surveillance Study and then "matched" with a randomly selected control drawn from all other eligible children. However, a number had to be excluded from each group (at-risk and control). Of those identified using the screening criteria, signed consent for follow-up had not been received for 1% at ascertainment. More than one third (36%) were not eligible for the 6-month follow-up because the study did not begin until they were past this age. In addition, to control for bias known to be associated with medical conditions, potential participants were excluded for the following reasons: (1) maternal medical problems (e.g., hepatitis, insulin-dependent diabetes, active sexual transmitted diseases, positive HIV status, sickle-cell disease) and (2) prenatal exposure to other known or potentially teratogenic substances (e.g., seizure medications, antidepressants). At 6 months, 8% of at-risk infants and 2% of controls were excluded, and at 12 months 10% of at-risk and 3% of controls were excluded, based on these medical criteria. Other drug use (e.g., cigarettes, marijuana, cocaine) was not an exclusionary factor, due to the high degree of correlation with alcohol use.

To control for both the birthweight and demographic factors known to be associated with developmental outcome, controls were matched on the following variables: (1) race, (2) hospital site (as a proxy for SES) and (3) birthweight for gestational age category (see above). Whenever an experimental infant had to be dropped because of exclusionary criteria or for noncompliance with the follow-up, the matching control had to be dropped as well. In contrast, an excluded control could be replaced by another, randomly selected from the Surveillance Sample, since there were often multiple control participants available for each at-risk infant. At 6 months, 35 matched mother-infant pairs ($n = 70$) were selected and, at 12 months, 68 pairs ($n = 136$); there were 55 families that participated both times.

To examine the effects of attrition and exclusion on sampling characteristics, comparisons were made between infant characteristics, maternal substance use and lifestyle variables of families selected and seen at 6 and 12 months and those who were seen at neither follow-up. Follow-up participants had a slightly longer gestation (3 days, $t = -2.02$, 118 df, $p < .05$) and were more likely to be born at the suburban hospital ($\chi^2 = 4.57$, 1 df, $p < .03$) than those selected who did not participate. Caregivers who did not participate had fewer years of school ($t = -3.09$, 125 df, $p < .003$) and were more likely to use cigarettes ($\chi^2 = 5.36$, 1 df, $p < .02$) and cocaine ($\chi^2 = 4.83$, 1 df, $p < .03$). There were no group differences for birthweight, infant's gender, mother's age, marital status, ethnic group, ounces of absolute alcohol per week (AA/wk), marijuana use or heavy drinking during pregnancy. In the at-risk group, there was one nonmaternal caregiver at 6 months and four at 12 months; all controls remained with their biological mothers.

Procedure

Participating caregivers were contacted by mail or by phone 2 months before infants were eligible for testing at 6 and 12 months. When necessary, the infant's age was corrected for prematurity (that is, < 37 weeks gestational age) by adding the number of weeks preterm to chronological age. Appointments were made for the time of day when caregivers reported that children were most likely to be alert and responsive. Transportation to the laboratory was provided as needed and participants were reimbursed $30 for their participation.

Following guardians' signing of the informed consent document (approved by the Emory University School of Medicine's Human Investigation Committee), information was collected from both caregivers and infants. Caregivers were interviewed by research interviewers and completed several questionnaires. Infants were tested by a psychologist using the Bayley Scales of Infant Development, Second Edition (BSID-II; Bayley, 1993). Infants were also weighed and measured by the testers during their visit to the laboratory, to obtain HC, body weight and length.

Maternal measures. Questionnaires given to caregivers included a structured interview asking about parental demographics, alcohol and tobacco use during pregnancy and currently, nursing status and parity. Average ounces of absolute alcohol per week (AA/wk) was then calculated using a standard quantity-frequency technique (Cahalan et al., 1969). Caregivers completed several other measures, including the Family Resource Scale (Dunst and Leet, 1988), the Family Support Scale (Dunst et al., 1988), the Symptoms Checklist-90-R (SCL-90-R; Derogatis, 1975) and the Parenting Stress Index-Short Form (Abidin, 1993). To control for possible differences in reading, consent forms and questionnaires were read to participants.

Infant measures of neurodevelopment and growth. The developmental test used, the BSID-II (Bayley, 1993), includes Mental (MDI) and Psychomotor (PDI) Index Standard Scores (mean [SD] = 100 [15]) and provides developmental age facet scores across four different clusters (cognitive, language, social and motor). The social cluster was omitted here because the number of items is limited for the age ranges sampled (three items at 6 months and one item at 12 months). The BSID-II also includes the Behavioral Rating Scale (BRS), scored by examiners to assess the quality, organization and stability of behavior during the exam. In addition to the total score, BRS items are clustered into three subscales: Orientation/Engagement, Emotional Regulation and Motor Quality. Percentile ranks on each are rated as "nonoptimal" (≤ 10th percentile), "questionable" (11th to 25th percentile), or "within normal limits" (≥ 26th percentile).

Infants were assessed by one of two clinical psychology graduate students blind to experimental group status. Interrater reliability, based on scores from videotaped administrations, using Cronbach's alpha was .95 for the BSID-II MDI and .85 for the BRS-total score.

Results

Selected sample characteristics

Data analyses were conducted on the matched samples (35 pairs at 6 months and 68 pairs at 12 months). Comparison of experimentals (those at risk) and controls were conducted using the *t* test for continuous data and chi-squares for categorical data. At-risk individuals and controls differed on only a few measures. Table 1 shows demographic characteristics of parents at each follow-up point.

Substance use. Because alcohol use was related to the selection criteria, the groups differed significantly on oz AA/wk both for the neonatal report of use during pregnancy (6 months, at-risk: mean [SD] = 2.92 [7.47], 6 months, controls: 0, $t = 2.31$, $p < .03$; 12 months, at-risk: mean [SD] = 2.41 [6.22], 12 months, controls: mean [SD] = 0.08 [0.49], $t = 3.07$, $p < .003$) and for the report of pregnancy use given at follow-up (6 months, at-risk: mean [SD] = 3.34 [5.45], 6 months, controls: mean [SD] = 1.18 [2.22], $t = 2.11$, $p < .04$); 12 months, at-risk: mean [SD] = 3.85 [7.06], 12 months, controls: mean [SD] = 1.06 [1.91], $t = 3.03$, $p < .003$). Greater alcohol use during pregnancy was reported at follow-up than at ascertainment in the hospital, a phenomenon observed in other samples (Ernhart et al., 1988; Jacobson et al., 1991). Women who reported heavy episodic drinking during pregnancy (≥ 5 drinks/occasion) also drank on more occasions (three to five times per month) than did those who did not report this pattern (one to two times per month) and did so during each trimester (6 month sample: $t = 3.22$, $p < .003$; 12 month: $t = 5.23$, $p < .0001$). Selected (at-risk) cases were significantly more likely than controls to smoke cigarettes (6 months: 62.9% vs 28.6%, $\chi^2 = 8.29$, 1 df, $p < .004$; 12 months: 60.3% vs 22.1%, $\chi^2 = 20.5$, 1 df, $p < .001$). Similar results were found for cocaine (6 months: 31.4% vs 2.9%, $\chi^2 = 10.06$, 1 df, $p < .002$; 12 months: 29.4% vs 1.5%, $\chi^2 = 20.33$, 1 df, $p < .001$) and marijuana (6 months: 28.6% vs 5.7%, $\chi^2 = 6.44$, 1 df, $p < .01$; 12 months: 20.6% vs 5.9%, $\chi^2 = 6.4$, 1 df, $p < .01$) but not for other drugs (i.e., sleeping pills, tranquilizers, antidepressants, heroin, LSD, Quaaludes, ICE, PCP). No differences were noted in comparisons of the psychosocial characteristics of respondents (SCL-90-R; Derogatis, 1988) or on the Parenting Stress Index (Abidin, 1993), with all test means in the average range. In the 12-month sample, perceived family support was lower ($t = 2.43$, $p < .02$) in the at-risk group.

TABLE 1. Caregiver characteristics[a]

Caregiver characteristics	6-month group ($n = 70$) At-risk ($n = 35$)	6-month group ($n = 70$) Control ($n = 35$)	12-month group ($n = 136$) At-risk ($n = 68$)	12-month group ($n = 136$) Control ($n = 68$)
Mother's age (yrs)	30.1	28.6	30.2	27.2
Previous pregnancies (no.)	3.5	3.2	3.4	3.1
Marital status (% married)	21.2	33.5	38.3	41.2
Father's age (yrs)	35.2	31.4	34.4	30.4
Father involved (%)				
During week	79.4	72.7	74.2	70.0
During weekend	81.8	84.8	72.3	74.2
Mother's education (%)				
Graduate/professional	14.29	5.71	7.4	10.3
Bachelor's degree	8.57	14.29	7.4	16.2
Associate degree	5.71	5.71	4.4	4.4
Some college	20.0	2.86	22.1	11.8
High school degree	20.0	51.43	30.9	36.8
< High School	31.43	20.0	27.9	20.6
Father's education (%)				
Graduate/professional	10.0	15.6	7.9	12.1
Bachelor's degree	13.3	9.4	14.3	13.6
Associate degree	0	3.1	0	3.0
Some college	26.7	21.90	15.9	15.2
High school degree	30.0	31.3	44.4	37.9
< High school	16.7	18.8	17.5	37.9
Income level (%)				
> $70,000	11.4	18.7	12.12	16.42
$50,000-70,000	8.6	12.5	9.09	8.94
$30,000-49,999	5.7	6.2	6.06	9.0
$10,000-29,999	14.3	15.6	22.7	19.4
< $10,000	60.0	46.8	50.0	44.3

[a]No comparisons statistically significant.

Infant characteristics

Approximately half of the sample was male (45.71%). There were no differences noted in infant birthweight (6 months: mean [SD] = 2666.12 [443.80] grams; 12 months: mean [SD] = 2668.92 [488.04]). The mean

gestational age was 38.71 weeks for both samples with no group differences observed. Approximately two thirds of the follow-up sample (61.8% to 65.7%) was black; this is significantly higher than the percentage in the surveillance sample (42.3%) from which it was selected.

Physical growth outcomes at 6 and 12 months

No significant differences between the groups were found on HC, height or weight using either continuous or categorical (< 10th percentile) indices of growth (Tables 2 and 3). With the exception of height at 12 months, all growth parameters were within normal limits (Hamill et al., 1979). Mean height at 12 months was < 5th percentile for both males and females in comparison to these standards.

When each of the three alcohol-related selection criteria was examined independently to determine if one was more useful in identifying growth retardation (Tables 4 and 5), no significant differences were found. In fact, at 12 months, a trend (χ^2 3.52, 1 df, $p < .06$, OR = 3.33) was found only on *current* HC for the infants who were identified as having disproportionately smaller HC at birth.

Behavioral outcome measures at 6 and 12 months

Tables 2 and 3 display the results of the Behavioral Rating Scale (BRS) completed at 6 and 12 months, respectively. In the 6-month sample, at-risk infants had significantly lower scores on the Emotional Regulation scale than did controls, suggesting poorer regulation of their emotional reactions to the testing experience. Infants who were selected as high risk due to high scores on the MSA Checklist or heavy episodic drinking were rated significantly lower than those in the control group on emotional reactivity, whereas only a trend was found for those who had a disproportionate HC (Tables 4 and 5). Overall, no differences were found between the groups on Orientation, Motor Quality or Total Behavior Rating at either age. However, when results were

TABLE 2. Outcomes at 6 months: At-risk/control (N = 70)

Developmental outcome	At-risk (n = 35)	Control (n = 35)
Physical outcomes		
HC (cm)		
Mean (SD)	43.2 (1.50)	43.1 (1.50)
< 10%	20%	22.90%
Height (in)		
Mean (SD)	25.4 (1.40)	25.7 (1.30)
< 10%	28.60%	31.40%
Weight (lbs)		
Mean (SD)	16.3 (2.0)	16.4 (2.0)
< 10%	28.60%	0.2%
Neurodevelopmental		
BSID-II MDI (mental)		
Mean (SD)	94.4 (7.30)	95.86 (7.00)
% delay	8.57%	8.57%
BSID-II PDI (motor)		
Mean (SD)	97.5 (15.60)	98.37 (11.20)
% delay	17.14%	8.57%
BSID-II cognitive facet		
Mean (SD)	49 (3.60)	49.14 (2.90)
BSID-II language facet		
Mean (SD)	7 (0.63)	7.4 (0.98)
BSID-II motor facet		
Mean (SD)	54.3 (6.80)	55.1 (4.50)
Behavior rating (BRS)		
Orientation		
Mean (SD)	39.6 (7.30)	41.9 (7.00)
% NO	42.9%	28.6%
Emotional Regulation*		
Mean (SD)	28.6 (4.70)	31.3 (4.60)
% NO	54.3%	30.0%
Motor Quality		
Mean (SD)	28.3 (3.90)	29.5 (4.90)
% NO	42.9%	37.1%
Total		
Mean (SD)	103.98 (15.10)	109.8 (11.70)
% NO	45.7%	30.0%

*$p < .05$.
Notes: HC = head circumference; NO = nonoptimal.

TABLE 3. Outcomes at 12 months: At-risk/control (N = 136)

Developmental outcome	At-risk (n = 68)	Control (n = 68)
Physical outcomes		
HC (cm)		
Mean (SD)	45.7 (2.80)	46.2 (1.50)
< 10%	25%	17.70%
Height (in)		
Mean (SD)	26.8 (1.10)	28.8 (2.00)
< 10%	35.30%	33.80%
Weight (lbs)		
Mean (SD)	21.6 (2.70)	21.5 (3.00)
< 10%	17.70%	23.50%
Neurodevelopmental		
BSID-II MDI (mental)†		
Mean (SD)	92.7 (12.20)	96.10 (11.70)
% delay	29.41%	13.24%
BSID-II PDI (motor)		
Mean (SD)	95.2 (15.10)	94.80 (13.30)
% delay	23.53%	20.59%
BSID-II cognitive facet†		
Mean (SD)	67.3 (8.30)	68.80 (3.80)
BSID-II language facet		
Mean (SD)	13.3 (1.80)	13.2 (1.50)
BSID-II motor facet		
Mean (SD)	89.9 (5.10)	90.8 (4.20)
Behavior rating (BRS)		
Orientation		
Mean (SD)	44.8 (5.60)	43.6 (6.90)
% NO	30.9%	23.5%
Emotional Regulation		
Mean (SD)	30.8 (4.50)	31.0 (4.50)
% NO	13.24%	20.59%
Motor Quality		
Mean (SD)	31.9 (3.50)	31.7 (2.70)
% NO	14.7%	8.8%
Total		
Mean (SD)	115 (10.70)	114.3 (12.40)
% NO	13.24%	20.59%

†$p < .02$.
Notes: HC = head circumference; NO = nonoptimal.

TABLE 4. Outcomes at 6 months: By selection criteria ($N = 70$)[a]

Developmental outcome	MSA Checklist ($n = 25$)	≥ 5 drinks/occ. ($n = 19$)	HC disprop. ($n = 4$)	Control ($n = 35$)
Physical outcomes				
HC (cm)				
Mean (SD)	43.1 (1.60)	43.2 (1.80)	43.6 (1.90)	43.1 (1.50)
< 10%	21.50%	20%	25%	22.86%
Height (in)				
Mean (SD)	25.4 (1.60)	25.1 (1.70)	25.1 (0.94)	25.7 (1.30)
< 10%	28%	31.60%	50%	31.40%
Weight (lbs)				
Mean (SD)	16.4 (2.10)	16.3 (2.40)	15.3 (1.10)	16.4 (2.00)
< 10%	28%	31.58%	25%	20%
Neurodevelopmental				
BSID-II MDI (mental)				
Mean (SD)	95 (6.10)	93.3 (8.10)	96 (4.30)	95.9 (7.00)
% delay	8%	10.50%	0%	8.57%
BSID-II PDI (motor)				
Mean (SD)	97 (11.40)	100.3 (18.60)	92.5 (11.10)	98.4 (11.20)
% delay	16%	10.50%	25%	8.57%
BSID-II cognitive facet				
Mean (SD)	49.2 (2.90)	48.5 (4.10)	49.8 (2.20)	49.1 (2.90)
BSID-II language facet				
Mean (SD)	7.1 (0.70)	6.9 (0.64)*	7 (0.00)	7.4 (1.00)
BSID-II motor facet				
Mean (SD)	54.2 (4.80)	54.8 (8.20)	37.5 (3.70)	55.1 (4.50)
Behavior rating (BRS)				
Orientation				
Mean (SD)	40.3 (6.80)	38.9 (8.00)	34.8 (4.60)*	41.9 (7.00)
% NO	56%	63.10%	100%	57.10%
Emotional Regulation				
Mean (SD)	28.7 (5.00)*	28.3 (5.10)*	27 (4.80)	31.3 (4.60)
% NO	56%	63.20%	75%	48.60%
Motor Quality				
Mean (SD)	28.3 (4.10)	28.5 (5.70)	26.75 (6.10)	29.5 (3.90)
% NO	56%	52.60%	75%	48.60%
Total				
Mean (SD)	104.5 (14.30)	103.2 (16.60)	95.5 (14.6)*	109.8 (11.70)
% NO	60%	63.16%	100%	65.71%

*$p < .05$.
[a]At-risk infant might meet more than one criterion. Overlap: All 3 criteria = 0; MSA Checklist and ≥ 5 drinks/occ. = 13; MSA Checklist and HC = 0; ≥ 5 drinks/occ. and HC = 0.
Notes: HC = head circumference; NO = nonoptimal.

broken down by selection criteria, those infants who had a disproportionately smaller HC were found to have lower BRS total scores and Orientation scores at 6 months, and at 12 months these infants had lower total scores on the BRS.

Neurodevelopmental outcome measures

Tables 2, 3, 4 and 5 display the BSID-II neurodevelopmental outcomes for both age groups. No differences were found for mental or motor development standard scores at 6 months. However, when at-risk 6-month infants were grouped based on the three selection criteria (Table 4), those whose mothers reported episodes of heavy drinking received significantly lower scores on the BSID-II language facet than did controls. At 12 months (Table 3), at-risk infants had significantly lower BSID-II cognitive scores and significantly more could be classified as showing developmental delays. When 12-month cases were broken down by selection criteria and compared to the controls (Table 5), those whose mothers scored high on the MSA Checklist were significantly more likely to have a MDI standard (mental) score below 85. Twelve-month outcome infants who were born with smaller HC had lower scores on the cognitive cluster. Trends for relationships between the HC and lower MDI scores ($t = 1.70$, $p < .09$) and a greater incidence of delay categorization (% NO) were also found ($\chi^2 = 3.02$, 1 df, $p < .08$).

Discussion

This study evaluated the usefulness of methods for early identification of infants at risk for FAS and other

TABLE 5. Outcomes at 12 months: By selection criteria ($N = 136$)[a]

Developmental outcome	MSA Checklist ($n = 50$)	≥ 5 drinks/occ. ($n = 31$)	HC disprop. ($n = 12$)	Control ($n = 68$)
Physical outcomes				
HC (cm)				
Mean (SD)	45.5 (3.20)	45.1 (3.80)	45.5 (2.10)	46.2 (1.50)
< 10%	28%	32.30%	41.7%[§]	17.70%
Height (in)				
Mean (SD)	28.6 (1.30)	28.4 (1.10)	28.2 (1.40)	28.8 (2.00)
< 10%	36%	38.70%	58%	33.80%
Weight (lbs)				
Mean (SD)	21.1 (2.90)	21.1 (2.90)	21.2 (3.60)	21.2 (3.00)
< 10%	22%	19.40%	17%	23.50%
Neurodevelopmental				
BSID-II MDI (mental)				
Mean (SD)	92.1 (12.30)[§]	93.3 (13.40)	90 (10.10)*	96.1 (11.70)
% delay	30%*	22.60%	33.3%*	13.20%
BSID-II PDI (motor)				
Mean (SD)	94.5 (15.50)	97 (16.70)	92.7 (13.20)	94.8 (13.30)
% delay	26%	29%	16.7%	20.60%
BSID-II cognitive facet				
Mean (SD)	67.2 (3.80)	67.4 (4.40)	66.3 (2.90)*	68.8 (3.80)
BSID-II language facet				
Mean (SD)	13.2 (1.90)	13.3 (1.80)	13.1 (1.70)	13.2 (1.50)
BSID-II motor facet				
Mean (SD)	89.6 (5.10)	90.3 (6.00)	88.8 (4.30)	90.8 (4.20)
Behavior rating (BRS)				
Orientation				
Mean (SD)	44.2 (5.80)	45.3 (5.70)	45.1 (5.90)	43.6 (6.90)
% NO	38%	25.80%	41.70%	33.80%
Emotional Regulation				
Mean (SD)	30.9 (4.60)	30.8 (4.8)	29.3 (4.70)	31 (4.50)
% NO	50%	48.40%	58.30%	50%
Motor Quality				
Mean (SD)	31.6 (3.70)	31.9 (4.10)	32.4 (3.60)	31.7 (2.70)
% NO	26%	22.60%	16.70%	26.50%
Total				
Mean (SD)	114.3 (11.00)	115.6 (11.80)	113.3 (10.2)*	114.3 (12.40)
% NO	40%	26%	58.30%	36.80%

[§]$p < .1$; *$p < .05$.
[a]At-risk infants might meet more than one criterion. Overlap: All 3 criteria = 1; MSA Checklist and ≥ 5 drinks/occ. = 20; MSA Checklist and HC = 1; ≥ 5 drinks/occ. and HC = 2.
Notes: HC = head circumference; NO = nonoptimal.

alcohol-related neurodevelopmental disorders. Three criteria were selected to identify those most at-risk from a predominantly growth-retarded cohort recruited from two metropolitan hospitals: one urban, one suburban. Selected infants differed significantly from controls matched on pertinent demographic variables (i.e., race, hospital site of birth [proxy for SES] and weight for gestational-age status). Comparisons of demographic and psychosocial characteristics, maternal psychopathology and infant demographics between those selected and matched controls yielded few group differences, suggesting that matching procedures effectively controlled these potentially confounding factors. Mothers of selected infants were significantly more likely than mothers of controls to be using cigarettes, marijuana and cocaine. This typical pattern of polydrug use indicates that caution must be used in attributing observed group differences only to the prenatal alcohol exposure since other drugs may affect outcomes as well. However, this finding does not detract from the usefulness of alcohol-related factors as indicators of risk in a screening process. The only additional pre-existing differences between groups were parental age and perceived family support, which are well established covariates of substance use (Bresnahan et al., 1992; Day et al., 1993). These factors may also contribute to negative impacts on neurodevelopment but are viewed as having mutually causal relationships (Loehlin, 1992) with maternal substance use and are, therefore, difficult to independently assess or separate from substance use effects.

Behavioral regulation and neurodevelopmental status

In comparison to controls, those selected as potentially

alcohol-affected had significantly lower scores on the Emotional Regulation scale of the BSID-II at 6 months of age; lower scores on the cognitive cluster of the BSID-II at 12 months of age; and were more likely to be classified as in the delayed category at 12 months. Thus, infants who were identified as being at risk for alcohol-related neurological damage were, in fact, more neurodevelopmentally compromised than others in this growth-retarded cohort. However, the overall incidence of developmental and behavioral regulation problems observed was relatively high among all the infants studied (see Tables 2 - 5) indicating that being smaller for gestational age is generally associated with a higher risk for neurodevelopmental compromise. Greater differences in outcome might be expected if selected infants were compared to children of average birthweight.

These results establish the usefulness of neonatal identification. The selection criteria used *in addition to* low birthweight identified children who were more likely to have neurodevelopmental compromise. When the selection methods were examined individually for their predictive utility, each method was found to be useful in predicting some features of neurodevelopmental compromise.

Infant head circumference

The disproportionately small head size criteria selected the fewest number of infants (4 at 6 months and 12 at 12 months); this made interpretation of the outcomes difficult, due to the low power and instability associated with results obtained from small samples as well as the possibility of spurious results due to multiple comparisons. However, the HC group presented with more neurodevelopmental compromise at both 6 and 12 months than those in the other groups. Less effective behavioral regulation was noted at both 6 months (a trend only) and at 12 months, with the continuity suggesting compromise in this area. At 12 months, lower cognitive cluster scores were found on the BSID-II. This method of flagging infants appears promising, but additional investigation is needed in a much larger sample. In addition, there are many causes of microcephaly, so this method is limited in identification of specific alcohol-related disorders.

Heavy episodic drinking

Heavy episodic drinking (≥ 5 drinks/occasion) during pregnancy is often associated with developmental deficits in later childhood (Abel, 1998; Streissguth et al., 1994). In this study, infants whose mothers reported such drinking patterns had lower scores on the Emotional Regulation scale and the language cluster score of the BSID-II at 6 months when compared to controls. However, at 12 months, this group was not significantly different on indices of cognitive functioning. Thus, during the first year, a persistent pattern of neurodevelopmental compromise was not demonstrated, suggesting that maternal reports of excessive alcohol consumption, although commonly used, may not be effective in identifying deficits that can be measured during infancy.

Maternal Substance Abuse Checklist

This CRI was developed as a tool for identifying women who are at risk for having an alcohol-affected child. Scores on this instrument did show different patterns between the two hospital sites (that differed vastly in the socioeconomic characteristics of their respective populations). However, the overall magnitude of the difference between total scores of each hospital site was small, and a cutoff of 7 (of 17 possible items) provided a meaningful way of delineating a subgroup from both samples that differed significantly from the typical range of scores. Compared to controls, infants who were selected based on their mothers having a high score on this measure had significantly lower Emotional Regulation scores at 6 months and a higher percentage of cognitive scores in the delayed range at 12 months. Therefore, this method alone was sufficient to identify infants who were at risk for neurodevelopmental compromise. Because of the items used in the MSA Checklist, this measure may be more specific for the effects of prenatal alcohol exposure than HC and more sensitive than heavy episodic drinking. However, this method of selection identified a relatively large sample of the infants as "cases." To determine the most effective cutoff point for prediction of later developmental status, additional research with a larger sample of children would be needed in order to examine the full continuum of checklist scores and provide the best estimate of hits, false positives, misses and true negatives that a given cutoff score would produce.

Physical growth during the first year

Growth retardation and small head circumference are well-established features of the FAS diagnosis. In this study, in which the level of prenatal alcohol use was relatively moderate, there was no specific relationship between these alcohol-related criterion and growth over the first year. However, the absence of growth effects in this sample of infants who were identified as being at risk for alcohol-related impairment may also be attributed to the reference sample from which they were selected. Since the majority of the sample was growth retarded and controls were matched on this dimension, both groups appeared to be equally likely to be developmentally compromised. The specificity found in developmental outcomes by the selection criteria used (cognitive and neurobehavioral but not growth) suggests that these instruments are useful in further defining the individuals who are likely to be alcohol affected from those who are growth retarded for other reasons.

Additional follow-up at a later point in development

would be useful in further assessing neurodevelopmental compromise among this sample of children. As individuals develop, increasing differentiation of cognitive abilities arises, allowing for assessments of global and specific deficits associated with prenatal alcohol exposure. Clearly, in this sample, the groups showed greater discrepancies at 12 months than they did at 6 months, suggesting that group differences are not uniform across developmental phases and may actually increase over time. Further differentiation in cognitive abilities over the course of their development may yield even greater discrepancies in the neurodevelopment of the individuals selected as cases and controls for this study and is needed to clarify the long-term predictive utility of these selection methods.

Appendix: Items on the Maternal Substance Abuse Checklist

1. Maternal age ≥ 24 years.
2. Number of births ≥ 3.
3. Chronic liver disease present.
4. Anemia diagnosed.
5. Began drinking alcohol < 16 years.
6. Drinks 3 or 4 times a week either before or during pregnancy.
7. Drinks ≥ 2 drinks per occasion either before or during pregnancy.
8. Reported drinking ≥ 5 drinks per occasion before pregnancy.
9. Reported drinking ≥ 5 drinks per occasion during pregnancy.
10. Drinks throughout pregnancy (does not stop when learns of pregnancy).
11. Told to drink less before she was pregnant.
12. Told to stop drinking before she was pregnant.
13. Has tried to quit drinking ever.
14. Reports having had withdrawal symptoms when trying to stop.
15. Reports ever having had social problems due to drinking.
16. Has a primary relationship with drinker.
17. Smokes currently.

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