

EFFECTS OF PRENATAL ALCOHOL EXPOSURE ON INFANT VISUAL ACUITY

R. COLIN CARTER, MD, SANDRA W. JACOBSON, PhD, CHRISTOPHER D. MOLTENO, MD, LISA M. CHIODO, PhD,
DENIS VILJOEN, MD, AND JOSEPH L. JACOBSON, PhD

Objective To examine the effects of prenatal alcohol exposure ascertained prospectively on infant visual acuity across a range of exposures and factors that mediate or moderate these effects.

Study design Infant visual acuity was examined in 131 Cape Coloured (mixed ancestry) maternal-infant pairs in Cape Town, South Africa. Drinking patterns were documented by maternal reporting during pregnancy. Grating acuity was assessed with Teller Acuity Cards (TAC) at 6.5 months after term. Data were analyzed by correlation, multiple regression, and analysis of variance.

Results Greater average daily prenatal alcohol exposure was related to poorer acuity, as indicated by lower TAC scores. The effect of alcohol on acuity was significant primarily for infants born to mothers ≥ 30 years of age at delivery, in comparison to infants born to younger mothers. This effect was not mediated by gestational age or birth size or attributable to alcohol-related neurocognitive deficits.

Conclusions This study linked prenatal alcohol exposure ascertained prospectively to poorer visual acuity in infancy. The results are consistent with clinical and animal evidence of alcohol-related disruption of the visual system. (*J Pediatr* 2005;147:473-9)

In the early 1970s, Jones and Smith¹ described a syndrome of prenatal growth deficiency, developmental delay, and specific craniofacial dysmorphism, which they termed *fetal alcohol syndrome* (FAS). Disorders of the eye were noted in the earliest reports of FAS, and case studies have documented numerous ophthalmologic abnormalities.²⁻⁷ In a case study of 30 children with FAS referred for ophthalmologic evaluation, 90% had some ophthalmologic abnormality, and more than half of those affected had impaired visual acuity.^{5,6} Another study found poorer acuity in 9 of 10 children with FAS.³

Previous studies on prenatal alcohol exposure reported poorer visual acuity but were limited to children diagnosed with FAS, only included small numbers of infants, and lacked quantitative documentation of maternal drinking levels. We examined the effects of heavy prenatal alcohol exposure in a prospective, longitudinal study in which maternal alcohol use was ascertained during pregnancy. Because prenatal alcohol exposure is associated with reductions in birth size and length of gestation,^{8,9} which can be related to developmental disabilities, we examined prenatal and postnatal growth and gestational age as potential mediators of observed effects of prenatal alcohol on visual acuity. Performance on the Fagan Test of Infant Intelligence (FTII),¹⁰ a measure of visual recognition memory and information processing speed predictive of later intellectual development,¹¹ was included in the analyses to test the hypothesis that poorer attention or developmental delay may mediate the effect of prenatal alcohol exposure on acuity. Case studies of white and Native American women found that each successive child born to a heavy-drinking mother was more severely impaired than the previous one,^{12,13} a pattern caused by maternal aging rather than parity in controlled animal experiments.^{14,15} Because maternal age was identified as an important moderator of fetal alcohol effects on a broad range of deficits in

From the Department of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, Detroit, Mich; Johns Hopkins University School of Medicine, Baltimore, Md; Department of Psychiatry, University of Cape Town School of Medicine, Cape Town; Department of Medical Genetics, University of Witswatersrand, Johannesburg, and Foundation for Alcohol Related Research, University of Cape Town, South Africa.

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Reprint requests: Sandra W. Jacobson, PhD, Department of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, 275 I E. Jefferson, Room 460, Detroit, MI 48207. E-mail: sjacobs@med.wayne.edu or colin.carter@childrens.tch.harvard.edu (R. Colin Carter, MD). 0022-3476/\$ - see front matter

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AA	Absolute alcohol	FTII	Fagan test of infant intelligence
AA/day	Absolute alcohol per day	TAC	Teller acuity cards
FAS	Fetal alcohol syndrome		

infancy and school-aged children in our Detroit and Cape Town cohorts,¹⁶⁻¹⁹ we examined whether maternal age moderated the relation between alcohol exposure and visual acuity.

Recent studies have documented a very high prevalence of FAS in the Cape Coloured (mixed ancestry) population in the Western Cape Province of South Africa. The Cape Coloured, mainly descendants of white European, Malaysian, Khoi (Hottentot), and black African ancestors, have historically comprised the large majority of workers in the wine-producing and fruit-growing region of the Western Cape. The high prevalence of FAS is a consequence of the very heavy maternal drinking during pregnancy commonly found in this community.

METHODS

Sample

The sample consisted of 131 infants (73 males, 58 females) born to women from the Cape Coloured community in Cape Town, South Africa, who are participating in a prospective study on the effects of heavy prenatal alcohol exposure on neurobehavioral development.²⁰ The mothers were recruited between July 1999 and January 2002 at the antenatal clinic of a midwife obstetric unit that serves an economically disadvantaged, predominantly Cape Coloured population. This clinic was selected for its high prevalence of heavy alcohol use on the basis of data collected from 6 midwife obstetric units in the Peninsula Maternity and Neonatal Service, which is associated with the University of Cape Town and serves 59.3% of the population.²¹

Each woman was interviewed regarding alcohol consumption both at the time of recruitment and at conception, using a timeline follow-back interview approach.²² Any woman averaging at least 1.0 oz absolute alcohol per day (AA/day), the equivalent of 2 standard drinks or about 30 mL AA/day, during the first trimester of pregnancy or reporting a history of at least 2 incidents of binge drinking per month during the first trimester was invited to participate in the study. Binge drinking was defined as consumption of at least 5 standard drinks on 1 occasion. The next woman initiating antenatal care at this clinic who drank <0.5 oz AA/day, did not binge drink during the first trimester, and whose gestational week of pregnancy was within 2 weeks of that of the previously recruited heavy-drinking participant was also invited to participate in the study. Women <18 years of age and those with diabetes, epilepsy, or cardiac problems requiring treatment were not invited to participate. Religiously observant Muslim women were also excluded because their religious practices prohibit alcohol consumption. Infant exclusionary criteria were major chromosomal anomalies, neural tube defects, multiple births, and seizures. Among the 131 infants for whom Teller Acuity Card (TAC) data were collected at 6.5 months after term, 61 (46.6%) were born to heavy-drinking women and 70 (53.4%) to abstainers and low level drinkers. Although heavy-drinking women were overrepre-

sented in this sampling design, prenatal alcohol exposure was treated as a continuous variable in all of the data analyses. Informed consent was obtained from each mother, and approval for human research was obtained from both the Wayne State University and the University of Cape Town human investigation committees.

Procedure

Infants were evaluated for visual acuity at 6.5 months, corrected for gestational age in cases of preterm birth. At the end of each visit, the mother received a small monetary compensation, a gift for her infant, and a photograph of herself with her infant.

Visual Acuity

Binocular visual acuity was assessed at 6.5 months on a resolution acuity test, the TAC,²³ which uses preferential looking to determine whether an infant can resolve individual lines in successively finer vertical gratings. Resolution acuity develops quickly during the first 6 months of life and then more slowly until adult acuity is reached at age 3 to 5 years.^{24,25} Trained testers were masked with respect to the infants' prenatal alcohol exposure. The TAC consists of a series of 16 rectangular cards, 28 cm by 60 cm in size, each of which contains a uniform gray background on which is imposed a 12.5-cm by 12.5-cm patch of black-and-white square-wave grating (black and white vertical stripes) that is located to the left or right of a central 4-mm peephole. The spatial frequency of the grating increases (ie, stripe width decreases) on successive cards from 0.23 to 38.0 cycles/cm in 0.5-octave steps. (An octave is a halving or doubling of stripe width).

During testing, the infant sat on the mother's lap and was shown the cards in order from wider stripes (0.64 cycles/cm) to finer and finer stripes at a distance of 55 cm. The examiner, who did not know which side the grating is on, looked through the peephole and judged which side of the card the infant preferentially fixated. The examiner then rotated the card 180 degrees and checked to see whether the infant looked to the opposite side of the card. The examiner could rotate the card by 180 degrees several times until a consistent preference was or was not exhibited. If a preference was exhibited, the examiner then verified whether the grating was on the side where the infant looked. When the infant failed to differentiate the grating from the gray background, the examiner retested the infant by going back to the previous card to confirm that the infant could make that discrimination. The examiner then returned to the card on which the infant failed to confirm that failure. The spatial frequency (in cycles/degree) of finest grating that the examiner judged that the infant could differentiate from the gray background was recorded as the infant's visual acuity score.

Visual acuity scores were converted to octaves by means of logarithmic (base2) values. Binocular acuity norms derived by Salomão and Ventura²⁴ from infants with no significant ocular disease were used to identify infants in our cohort with acuity scores below the fifth percentile at 6.5 months (ie, <3.38

cycles/degree). Correlational and regression analyses were performed on the octave scores; means are reported as cycles/degree and standard deviations in octaves.

Alcohol and Drug Use Data

Each mother was interviewed regarding her pregnancy alcohol and drug use at recruitment, at a follow-up antenatal visit, and when the infant was 1 month old. Almost all of the interviews were conducted in Afrikaans. During recruitment, the mother was asked about her drinking on a day-by-day basis during a typical 2-week period around the time of conception, with recall linked to specific times of day and activities. If her drinking had changed since conception, she was also asked about her drinking during the past 2 weeks and when her drinking had changed. At the follow-up antenatal visit, the mother was again asked about her drinking during the previous 2 weeks. If there were any weeks since the recruitment visit when she drank greater quantities, she was asked to report her drinking for those weeks as well. At the 1-month post-term visit, the mother was asked about her drinking during a typical 2-week period during the latter part of pregnancy, as well as her drinking during any weeks during that period when she drank greater quantities. Volume was recorded for each type of alcohol beverage consumed each day and converted to oz of absolute alcohol (AA) using multipliers proposed by Bowman et al²⁶ (liquor—0.4, beer—0.04, wine—0.2). Six summary measures were constructed—average AA/day at conception, AA/day averaged during pregnancy, AA per drinking day (quantity per occasion) at conception and during pregnancy, and proportion drinking days (frequency) at conception and during pregnancy.

In addition to the quantitative alcohol interview, the alcohol module of the Diagnostic Interview Schedule²⁷ was administered to each mother at the antenatal interview to determine whether she met Diagnostic and Statistical Manual of Mental Disorders—Fourth Edition (DSM-IV) criteria for alcohol abuse or dependence. Each mother was also asked at both the antenatal and postnatal interviews how many cigarettes she smoked per day and how often she used marijuana, inhalants (eg, glue or solvents), heroin, cocaine, mandrax, sedatives, or other drugs during pregnancy.

FAS Diagnosis

The infants were examined at 1, 12, or 13 months for presence of alcohol-related dysmorphic features by 2 dysmorphologists trained by Kenneth L. Jones, MD, and his colleagues to assess FAS in a previous South African study.²⁸ Frontal and side view facial photographs taken at 12 months post-term of each of the infants were also reviewed by Dr. Jones and Nathaniel Khaole, MD, for alcohol-related craniofacial dysmorphism. Children with the facial features characteristic of FAS (small palpebral fissures, flat midface, and smooth philtrum), significant growth retardation (<10th percentile for height and weight or <3rd percentile for head circumference), and evidence of poor central nervous system function were diagnosed as having FAS.

Control Variables

Data were obtained on a broad range of control variables, including maternal age, years of education, marital status, parity, maternal depression, and infant sex. Prenatal control variables also included maternal smoking and illicit drug use during pregnancy. Birth weight and head circumference were obtained from hospital medical records. Gestational age at birth was calculated from early pregnancy ultrasound examination or expected date of confinement when ultrasound data were not available. Weight, length, head circumference, and the FTII were measured at 6.5 months. The FTII consists of 10 problems, in which the infant is shown 2 identical target photographs for a fixed period of time and is then shown the familiar target paired with a novel one. Novelty preference (the proportion of looking time devoted to the novel stimulus) provides an index of visual recognition memory. The mean duration of the infant's visual fixations to the stimuli provides a measure of information processing speed.

Data Analysis

Before analysis, all variables were checked for normality of distribution. Average alcohol use per day at conception and during pregnancy were positively skewed (skew >3.0) and were normalized by means of log (X + 1) transformation. Pearson correlation analysis was used to determine which control variables should be included in multivariate analyses to control for potential confounding. Because a control variable cannot be the true cause of an observed deficit unless it is related both to exposure and outcome,²⁹ association with either exposure or outcome can be used as the criterion for inclusion in a multivariate analysis to control for confounding. In this study, control variables were selected in relation to outcome, which has the additional advantage of increasing precision by also including covariates unrelated to exposure.³⁰ We planned to assess the effect of each alcohol measure on acuity in a multiple regression analysis, adjusting for the effects of the potential confounders, as necessary. To assess mediating effects of gestational age and prenatal and postnatal growth, each regression analysis was rerun, adding each of the hypothesized mediators (gestational age at birth, birth weight and head circumference, and weight, length, and head circumference at 6.5 months) in separate analyses. In these analyses, the potential confounding variables and drinking during pregnancy were entered at the first step, the potential mediator at the second step. To determine whether maternal age moderated the effect of alcohol exposure on visual acuity, Pearson correlation analysis was used to determine the relation of alcohol exposure to visual acuity in infants whose mothers were either < or ≥ 30 years of age at delivery.

RESULTS

Sample

The mothers in the cohort were very poorly educated; only 24 (18.3%) had completed high school (Table I). Almost

Table I. Sample characteristics (n = 131)

	Mean or %	SD	Range
Maternal characteristics			
Age at delivery	27.3	6.4	18.4-43.8
Years of school completed	8.7	2.5	0.0-12.0
Married (%)	32.0	—	—
Parity	2.2	1.3	1.0-8.0
Infant characteristics			
Birth			
Sex (% female)	44.0	—	—
Gestational age (wk)	38.6	2.3	29.1-43.0
Weight (g)	2879.1	587.0	1130-4240
Weight percentile*†	32.8	29.5	0.5-90.3
Head circumference (cm)	32.8	2.0	23.0-36.0
Head circumference percentile*†	20.0	20.9	0.0-77.6
6.5-month visit			
Postnatal age at visit (mo)	7.1	0.6	5.6-9.4
Corrected age at visit (mo)	6.8	0.5	5.2-7.9
Weight (kg)‡	7.8	1.0	5.1-10.0
Weight percentile*‡	42.7	32.0	0.0-98.3
Length (cm)‡	67.4	2.6	60.0-73.0
Length percentile*‡	44.6	30.8	0.0-97.9
Length for weight percentile*‡	50.5	31.8	0.0-99.2
Head circumference (cm)‡	43.5	1.2	39.8-46.2
Head circumference percentile*‡	48.4	31.7	0.0-99.4
Number of weeks breast-fed‡	24.3	11.4	0.0-37.3
Visual acuity: cycles/degree§	6.4	0.6	2.4-13.0

*Based on percentiles from the Centers for Disease Control and Prevention.

†Not reported for 24 infants who were premature (gestational age at birth <37 weeks).

‡Not assessed for 1 infant.

§Based on TAC test.¹¹

||Calculations made using a logarithmic (base2) transformation on cycles/degree. Values for mean and range have been back transformed to cycles/degree; SD in octaves.

a third (30.5%) were 30 years of age or older at delivery, 47 (35.9%) were primiparous, and the majority (93.0%) breast-fed their infants. To date, among the Cape Coloured population, there is a much lower incidence of HIV than in black African mothers³¹ and, to the best of our knowledge, none of the infants in the sample was HIV positive.

Twenty-four infants (18.3%) were born preterm (gestational age <37), but only 2 were born at <32 weeks gestation. All of these preterm infants were subsequently tested at 6.5 months, corrected for gestational age. Twenty-five infants (19.1%) were low birth weight (<2500 g), 2 (1.5%) of whom were very low birth weight (<1500 g), with 1 born at 29.1 weeks and another infant who weighed 1240 g who was born at 33.9 weeks gestation. At the 6.5-month visit, 19 infants (14.6%) were below the 10th percentile for length and 27 (20.8%) for weight, and 13 (10.0%) were below the 5th percentile for head circumference. Sixteen infants (12.2%) fell below the 5th percentile for vision on the TAC procedure.

Table II. Maternal alcohol, drug use, and smoking

	N	Mean	% SD	Range
Daily average (oz AA)*				
At conception	68	1.5	1.7	0.02-11.6
During pregnancy	74	0.9	1.0	0.01-10.3
Average per drinking day (oz AA)*				
At conception	68	4.3	2.7	0.3-15.4
During pregnancy	74	3.2	2.0	0.2-10.3
Number of drinking days/week*				
At conception	68	2.1	1.4	0.02-7.0
During pregnancy	74	1.4	1.4	0.004-7.0
Alcohol abusing (%)†‡	109	11.0	—	—
Alcohol dependent (%)†‡	109	22.9	—	—
Cigarettes smoked per day*	92	7.5	6.0	0.4-40.0
Marijuana use (days/week)*	14	2.4	2.0	0.03-7.0

*Consumers only.

†Based on DSM-IV criteria.

‡Missing for 22 women.

No sex-related differences were found for acuity, $t(131) = -0.492, P > .20$.

Alcohol and Drug Use During Pregnancy

Half of the women (51.9%) reported drinking at conception, with slightly more (56.5%) drinking during pregnancy (Table II). As in other studies of pregnant women,³² these mothers reported reducing their alcohol consumption during pregnancy. However, although they reduced the number of days they drank by about a third, the women continued to drink at risk levels of on average 6.4 drinks per occasion during pregnancy. Eleven percent met DSM-IV criteria for alcohol abuse and an additional 22.9% for alcohol dependence. More than two thirds of the women (70.2%) reported smoking cigarettes, with one fifth smoking an average of 10 or more cigarettes per day. Marijuana and mandrax use was rare, and no women reported using inhalants (eg, glue or solvents), heroin, cocaine, sedatives, or other drugs during pregnancy.

Alcohol Effects on Visual Acuity

Alcohol exposure during pregnancy was significantly related to reductions in birth weight and 6.5-month weight and length but not to gestational age at birth (Table III). Twenty-two infants (16.8%) met criteria for a diagnosis of FAS. Six of these infants (27.3%) had TAC scores below the fifth percentile, compared with only 10 of the 107 (9.3%) infants without FAS, $\chi^2(1) = 7.80, P < .005$. The children in the bottom 5th percentile all had acuity scores of 3.2 cycles/degree or lower.

When visual acuity was examined as a continuous measure, none of the control variables were related to it at $P < .10$, and therefore none were controlled statistically in the data analyses. Poorer acuity at 6.5 months was associated with higher average daily alcohol consumption at conception and

Table III. Relation of prenatal alcohol exposure and FAS to visual acuity, gestational age, and growth (n = 131)

	Acuity	Gestational age	Birth weight	Birth head circumference	6.5-month weight	6.5-month length	6.5-month head circumference
Absolute alcohol/day							
At conception	-.21 [‡]	-.11	-.31 [§]	-.16 [*]	-.18 [†]	-.21 [†]	-.07
During pregnancy	-.23 [‡]	-.08	-.30 [§]	-.16 [*]	-.23 [‡]	-.24 [‡]	-.09
Drinks/occasion							
At conception	-.12	-.08	-.25 [‡]	-.10	-.14	-.24 [‡]	-.07
During pregnancy	-.14	-.12	-.29 [§]	-.14 [*]	-.17 [*]	-.25 [‡]	-.12
No. drinking days/week							
At conception	-.23 [‡]	-.11	-.30 [§]	-.16 [†]	-.14	-.12	-.04
During pregnancy	-.26 [‡]	-.10	-.34 [§]	-.21 [†]	-.28 [†]	-.21 [†]	-.12
Diagnosis of FAS	-.38 [§]	-.29 [§]	-.45 [§]	-.35 [§]	-.46 [§]	-.40 [§]	-.27 [‡]

Values are Pearson r's.

* $P < .10$.

† $P < .05$.

‡ $P < .01$.

§ $P < .001$.

during pregnancy (Table III). Although the amount of alcohol consumed on a given occasion was not related to acuity, infants born to mothers who binge drank were more likely to have acuity values below the 5th percentile than infants born to mothers who did not binge drink, $\chi^2(1) = 7.80, P < .005$.

Among the 10 infants with low TAC scores who did not meet the diagnostic criteria for FAS, 4 were born to mothers who reported binge drinking during pregnancy and 1 to a mother who drank an average of 1.9 oz AA/day (3.8 standard drinks) during pregnancy. The mother of 1 infant, who was diagnosed with FAS and whose TAC score was 2.4 cycles/degree, reported consuming 5.1 oz AA (10.2 standard drinks) per occasion. Although the mother of the other infant with a TAC score of 2.4 denied drinking during pregnancy, she met DSM-IV criteria for alcohol abuse and reported very heavy drinking (5.8 oz AA/occasion) during the month immediately before becoming pregnant. Frequency of drinking (proportion drinking days) both at conception and during pregnancy was also associated with poorer acuity. The relation of pregnancy drinking to acuity was dose-dependent, with effects clearly evident in those women whose drinking averaged at least 0.5 oz AA/day (Figure), $F(3,127) = 3.5, P < .05$. Not surprisingly, acuity was significantly poorer in the children diagnosed with FAS, $t(129) = 2.69, P < .01$.

Given that prenatal alcohol exposure is associated with reduced fetal⁸ and postnatal growth,⁹ the hypothesis that the effect of this exposure on acuity might be mediated by impaired somatic growth was tested by multiple regression analysis. The relation of pregnancy drinking to acuity was virtually unchanged when gestational age and birth size were included in the analysis but was reduced slightly by the inclusion of 6.5-month size, indicating that the poorer acuity seen in relation to prenatal alcohol exposure might relate, in part, to delayed postnatal development associated with slow somatic growth (Table IV). By contrast, the inclusion of

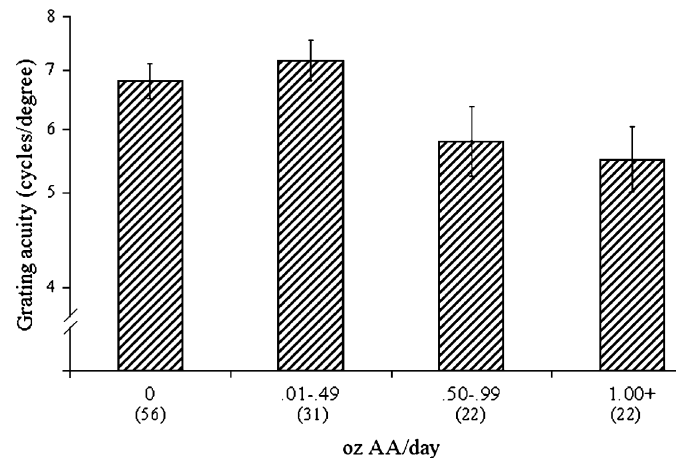


Figure. Relation of binocular visual acuity to four levels of drinking during pregnancy. Octave, which was computed by performing a logarithmic (base2) transformation on cycles/degree, has been back transformed to the original cycles/degree units on the y-axis. Group Ns are shown in parentheses.

measures of cognitive performance on the FTII did not mediate the effect of prenatal alcohol exposure on acuity, suggesting that the effect on acuity was not due to developmental delay, poorer attention, or ability to respond appropriately to the visual assessment procedure.

Table V examines maternal age as a potential moderator of the effect of prenatal alcohol on acuity. Although infants born to older mothers comprised only about one third of the cohort, the relation of daily alcohol exposure to visual acuity was seen primarily in the infants born to mothers 30 years of age or older. As expected, maternal age was highly associated with years of drinking in this cohort, $r = .59, P < .0001$. However, there were no significant differences in average daily alcohol intake between the 2 groups at conception, $t(129) = -0.54$, or during pregnancy, $t(129) = -0.24$, or in

Table IV. Effect of alcohol (AA/day during pregnancy) on acuity controlling for hypothesized mediating variables (n = 131)

Controlling for	R	β^*
Gestational age, birth weight, and head circumference	-.23 [‡]	-.25 [‡]
6.5-month weight, length, and head circumference [§]	-.25 [‡]	-.21 [†]
FTII—novelty preference and duration visual fixation	-.23 [‡]	-.22 [†]

*Effect of alcohol on acuity, controlling for potential mediators.

† $P < .05$.

‡ $P < .01$.

§Data missing for 1 infant.

consumption per occasion at conception, $t(129) = 0.75$, or during pregnancy, $t(129) = 0.10$, indicating that the greater vulnerability of the infants born to older mothers was not attributable to heavier drinking in older mothers.

DISCUSSION

This study is the first to prospectively document the impact of very heavy alcohol use during pregnancy by segments of the Cape Coloured population on infant development. The large number of infants with FAS born to the heavy drinking women in this cohort is consistent with the very high incidence reported in a retrospective study of Cape Coloured children entering elementary school, which was conducted in a more rural, grape-growing region of South Africa,²⁸ and extends those findings to show that heavy alcohol use and alcoholism during pregnancy persists among some subgroups of this population who have moved to urban areas.

We found that greater average daily prenatal alcohol exposure is related to poorer acuity, as indicated by lower TAC scores. Because a complete eye examination was not conducted on these infants, it is not possible to know the source of the alcohol-related lower acuity scores, such as refractive error, retinal changes, or central nervous system abnormalities. Our results are consistent with clinical case reports of poor visual acuity in children with FAS.³⁻⁷ We examined whether lower TAC scores among alcohol-exposed infants might be due to a developmental delay that affects the infant's ability to attend appropriately to the visual acuity cards. But the effect of prenatal alcohol exposure on acuity was independent of the infant's performance on the FTII, a valid measure of infant visual information processing that also depends on the infant's ability to attend to visual stimuli. The failure of gestational age and birth size to mediate the effect of prenatal alcohol on acuity suggests that the acuity defect was not attributable to poorer prenatal somatic growth. On the other hand, the acuity deficit seen at 6.5 months might be due to a maturational deficit or delay in the visual system and might therefore not be permanent. Predictive validity of the TAC for later acuity has

Table V. Maternal age ≥ 30 years as a moderator of the effect of prenatal alcohol exposure on infant visual acuity

	Age < 30 (N = 91)	Age ≥ 30 (N = 40)
Absolute alcohol/day		
At conception	-.14	-.33 [†]
During pregnancy	-.09	-.40 [‡]
Drinks/occasion		
At conception	-.05	-.25 [*]
During pregnancy	-.03	-.30 [*]
Number of drinking days/week		
At conception	-.13	-.35 [†]
During pregnancy	-.09	-.43 [‡]

Values are Pearson r 's.

* $P < .10$.

† $P < .05$.

‡ $P < .01$.

been demonstrated by Mash and Dobson.³³ However, the utility of the 6-month TAC as a screening instrument for alcohol-related ocular deficits depends on the degree to which TAC performance is related to ocular status at 6 months and predictive of later visual system anomalies, which needs to be assessed by ophthalmologic examination during childhood.

The effect of alcohol exposure on acuity was seen primarily in infants whose mothers were 30 years or older at delivery, even though the older mothers did not drink larger quantities of alcohol. This finding is consistent with previous research implicating maternal age as an important moderator of alcohol effects in animal studies,¹⁵ case reports of both white¹² and Native American¹³ children with FAS, and our previous research conducted on a moderate-to-heavily exposed, longitudinal Detroit cohort indicating increased vulnerability on numerous endpoints in children born to mothers 30 years of age or older.^{17,18} This increased vulnerability may be attributable to physiological changes in the mother relating to the aging process or to consequences of chronic drinking over a more prolonged period. Age-related increases in the ratio of maternal body fat to water lead to higher peak blood alcohol concentrations per unit dose of ethanol consumed, exposing the fetus of the older mother to higher doses.³⁴ A recent laboratory study found that exposure of female mice to daily heavy doses of alcohol before conception resulted in lower offspring body weights, ovarian anomalies, and fewer follicles that reached maturity, even when the animals were not exposed to alcohol during gestation,³⁵ suggesting that a longer history of alcohol abuse may reduce embryonic and fetal viability.

These findings suggest that the TAC is a useful tool for screening for adverse effects of prenatal alcohol exposure on acuity. Particular attention needs to be given to screening infants born to older mothers, who are at higher risk of damage to the ocular system from their mothers' alcohol use during pregnancy. An in-depth ophthalmologic evaluation of the

infants in this study during childhood is necessary to determine the nature of the visual abnormalities associated with fetal alcohol exposure and the degree to which the screening information from the TAC is indicative of these deficits.

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