

1 U01 AA014790-01

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Project Title: Identification of FASD in South African Children

PROGRESS REPORT SUMMARY

a. *Specific Aims*—Because only the first 3 years of the proposed 5-year project were funded, only the first of the two waves of child testing planned for this study will be conducted. The Specific Aims presented in the original grant proposal remain unchanged but will be studied in only one wave of data collection, rather than two.

b. *Studies and Results*.

This project, which is part of the Collaborative Initiative on Fetal Alcohol Spectrum Disorders (CIFASD) (RFA No. AA-03-002), entails a 5-year follow-up of a cohort of children and mothers recruited during pregnancy in 2000-2002. Implementation of the project began in January (the 4th month of the first grant year) as planned. During the first 3 months, our Cape Town-based research staff succeeded in locating all but one of the families from the first half of the cohort, and all those who were contacted agreed to participate in the follow-up assessment. In February, Drs. S. and J. Jacobson traveled to San Diego State University to meet with neuropsychologists from several of the CIFASD projects to develop a common test battery to be administered at all project sites. Because our project is the only one assessing preschool-age children, only a subset of the battery developed for school-age children will be administered, including the Leiter nonverbal intelligence test, the Beery Test for Visual-Motor Integration, the NES-3 continuous performance sustained attention test, the Grooved Pegboard fine motor test, and the Edinburgh Handedness Test.

In March, Andrea Hay, M.A., our clinical psychologist child examiner in Cape Town, traveled to the U.S. to be trained to perform the 5-year child assessments. She worked initially in our laboratory at Wayne State University to learn to administer the alcohol interviews to the mother and the Day-Night Test, an executive function test for preschool-age children. Drs. S. and J. Jacobson then traveled to University of Toronto together with Ms. Hay to meet with Dr. Philip Zelazo and learn to administer his executive function tests that have been adapted for preschool children: the Preschool Card Sorting Test, Preschool Gambling Test, and Go-No-Go computer task. They then traveled to the University of Delaware, where Ms. Hay worked for 4 days with Dr. Mark Stanton to learn to administer his eyeblink conditioning task and with Dr. Nancy Jordan to learn to administer her preschool arithmetic tasks. Ms. Hay then returned to Cape Town, where she pilot tested these assessments with 12 non-study children from the same community. Drs. S and J. Jacobson spent 2 weeks in April working with Ms. Hay in Cape Town to refine and adapt the procedures for administration of these tasks, as well as procedures for administering the Leiter test, the Edinburgh Handedness Scale, and eyeblink conditioning, to the children in this cohort, who come from very impoverished backgrounds. Drs. S and J. Jacobson also worked with Co-PI Dr. Christopher Molteno, a developmental pediatrician who is assessing psychopathology, stress, and spousal abuse in the mothers, and Deborah Price, a research nurse, who administers the maternal interviews pertaining to demographic background and alcohol and drug use.

Assessment of the children and the mothers in the cohort began on May 17, 2004. Six children and their mothers from the cohort have been assessed to date (June 17). The children, some of whom were heavily exposed to alcohol prenatally, all seem comfortable with the assessment procedures and generally seem to enjoy them. Earlier this month, Drs. S. and J. Jacobson traveled to the laboratory of Dr. Elizabeth Spelke at Harvard University, to obtain information about two innovative assessments of preschool number processing, the Give-a-Number Test, which assesses the mastery of small numbers (1-4), which emerges gradually during this age period, and the Dot Comparison task, which assesses the child's intuitive sense for large quantities, which also develops during this period. These new tasks will be added to the battery shortly.

Although it is too early in the study to begin to analyze the data, we are continuing to analyze data from the infant phase of this study, some of which are being presented at this year's Research Society on Alcoholism meeting. In one study, we found a strong linkage between prenatal alcohol exposure and iron deficiency anemia (IDA); 68% of the most heavily exposed infants met criteria for IDA, compared to only 38% in the infants born to abstainers or light drinkers. Both prenatal alcohol exposure and IDA were associated with smaller size at 6 and 12 months postpartum, and data from a path analysis suggested that the effect of prenatal alcohol on postnatal growth retardation may be mediated, in part, by IDA. In a second study, Dr. Molteno found that prenatal alcohol exposure and iron deficiency anemia were both associated with poorer mother-infant interaction, greater infant withdrawal, and poorer attachment, especially the disorganized (D) pattern. But, by contrast to postnatal growth retardation, these effects were independent; neither was mediated by the other. For her doctoral dissertation, Ms. Hay has examined the relation between prenatal alcohol exposure and infant-mother attachment. She found a relation between pregnancy drinking and less secure attachment, which appears to be mediated by the quality of the social environment. However, the relation of prenatal alcohol to disorganized attachment remained significant, even after controlling for socioenvironmental influences, suggesting that alcohol may impact directly on neural substrates that influence the development of disorganized attachment. A fourth study examined the degree to which immediate refrigeration and freezing are critical to the preservation of the meconium specimens, which we have used to assess concentrations of fatty acid ethyl esters (FAEEs), metabolites of alcohol, which provide a biomarker of maternal drinking during pregnancy.

c. *Significance*—The impressively high rates of iron deficiency among the infants heavily exposed to alcohol prenatally is consistent with animal experimental data suggesting that alcohol may interfere with iron metabolism *in utero*. It is of interest that, although our data suggest that iron deficiency anemia may play a role in mediating the effect of prenatal alcohol on postnatal growth retardation, the effects of alcohol on affective function appear to be independent of iron status. It is also of interest that, although some of the impact of prenatal alcohol on infant-mother attachment is mediated by socioenvironmental factors, the association with disorganized attachment appears to be affected more directly by the intrauterine impact of this exposure on brain development.

d. *Plans*—Data collection, scoring, and data entry will be the principal focus of this study during Year 2. We expect to assess approximately 75 children and mothers during that period.

e. *Publications*

Bearer, C.F., Jacobson, J.L., Jacobson, S.W., Barr, D., Croxford, J., Molteno, C.D., Viljoen, D.L., Marais, A.S., Chiodo, L.M., & Cwik, A.S. (2003). Validation of a new biomarker of fetal exposure to alcohol. Journal of Pediatrics, 143, 463-469.

Jacobson, J.L., & Jacobson, S.W. (2003). Effects of prenatal alcohol exposure on child development. Alcohol Research and Health, 26, 282-286.

Croxford, J., Jacobson, S.W., Carr, L., Li, T.-K., & Jacobson, J.L. (2003). Protective effects of the ADH2*3 allele in African-American children exposed to alcohol during pregnancy. Alcoholism: Clinical and Experimental Research, 27, 39A.

Armony-Sivan, R., Jacobson, S.W., Molteno, C.D., Carter, R.C., Viljoen, D., & Jacobson, J.L. (2004). Does iron deficiency anemia mediate the relation of fetal alcohol exposure to postnatal growth? Alcoholism: Clinical and Experimental Research.

Croxford, J., Jacobson, J.L., Bearer, C.F., Jacobson, S.W., Molteno, C.D. & Viljoen, D. (2004). The influence of variable storage conditions in the preservation of meconium specimens used for assessment of FAEEs in neonates prenatally exposed to alcohol. Alcoholism: Clinical and Experimental Research.

Hay, A.M., Jacobson, S.W., Molteno, C.D., Viljoen, D., & Jacobson, J.L. (2004). Alcohol exposure and infant-mother interaction in a South African community. Alcoholism: Clinical and Experimental Research.

Molteno, C.D., Jacobson, S.W., Hay, A.M., Armony-Sivan, R., Carter, R.C., Marais, A.S., Viljoen, D.L., & Jacobson, J.L. (2004). Iron deficiency anemia and socioemotional development in parentally alcohol exposure infants. Alcoholism: Clinical and Experimental Research.

Carter, R.C., Jacobson, S.W., Molteno, C.D., Viljoen, D., Chiodo, L.M., & Jacobson, J.L. (revise/resubmit). Effects of prenatal alcohol exposure on infant visual acuity. Journal of Pediatrics.