# Maternal Risk Factors for Fetal Alcohol Syndrome in the Western Cape Province of South Africa: A Population-Based Study

Phillip A. May, PhD, J. Phillip Gossage, PhD, Lesley E. Brooke, BA(Hons), Cudore L. Snell, DSW, Anna-Susan Marais, RN, Loretta S. Hendricks, Julie A. Croxford, RN, BA(Hons), and Denis L. Viljoen, MD

The search for specific maternal risk factors for fetal alcohol syndrome (FAS) has been ongoing for more than 2 decades via prenatal clinic 1-6 and epidemiological studies. 7-10 Population-based research is particularly helpful in identifying traits of the very highest-risk mothers—those who have borne children with full-blown FAS—and in designing prevention strategies. 10-14

FAS has been associated with heavy, episodic (binge) drinking that produces high blood alcohol concentration (BAC); advanced maternal age; high gravidity and parity; unstable marital status; cigarette use; and use of other drugs. 5,15-18 In the United States, higher FAS rates are reported among Black and American Indian women, lowsocioeconomic status (SES) groups, people with high scores on various alcohol abuse assessment tools, and women with alcoholic male partners. 19-24 Studies of mothers of children with fetal alcohol spectrum disorder (FASD; referred to by the Institute of Medicine 18 as FAS, partial FAS, alcohol-related birth defects, and alcohol-related neurodevelopmental deficits) point to a doseresponse effect. The probability of anomalies such as microcephaly, craniofacial defects, and behavioral problems depends on the level of alcohol exposure as modified by certain maternal characteristics, such as those on which this article reports.<sup>5,25-28</sup> The rate of FAS in US children is 0.05 to 2.0 per 1000 births.29 All levels of FASD affect, at minimum, 1% of the birth population.30 The highest rates of FAS in the world have been reported in the Republic of South Africa. The rate of full-blown FAS alone has been reported to be 46 cases per 1000 births in the Western Cape Province.8 Current research is documenting even higher rates in Western Cape Province 31 and high rates elsewhere in South Africa.32

Objectives. We defined risk factors for fetal alcohol syndrome (FAS) in a region with the highest documented prevalence of FAS in the world.

Methods. We compared mothers of 53 first-grade students with FAS (cases) with 116 randomly selected mothers of first-grade students without FAS (controls).

Results. Differences between case and control mothers in our study population existed regarding socioeconomic status, religiosity, education, gravidity, parity, and marital status. Mothers of children with FAS came from alcohol-abusing families in which heavy drinking was almost universal; control mothers drank little to no alcohol. Current and past alcohol use by case mothers was characterized by heavy binge drinking on weekends, with no reduction of use during pregnancy in 87% of the mothers. Twenty percent of control mothers drank during pregnancy, a rate that declined to 12.7% by the third trimester. The percentage who smoked during pregnancy was higher for case mothers than for control mothers (75.5% vs 30.3%), but the number of cigarettes smoked was low among case mothers. The incidence of FAS in offspring of relatively young women (28 years) was not explained by early drinking onset or years of drinking (mean, 7.6 years among case mothers). In addition to traditional FAS risk factors, case mothers were smaller in height, weight, head circumference, and body mass index, all anthropomorphic measures that indicate poor nutrition and secondgeneration fetal alcohol exposure.

Conclusions. Preventive interventions are needed to address maternal risk factors for FAS. (Am J Public Health. 2005;95:1190–1199. doi:10.2105/AJPH.2003. 037093)

FAS is associated with low SES among subpopulations<sup>23,33</sup> in developed and developing countries.<sup>9,34</sup> In South Africa,<sup>8,35</sup> mothers of children with FAS were of lower SES than were control mothers. In 1 US study that compared women of differing SES who consumed 12 drinks daily, the rate of FAS was 45 times greater in women of low SES than in women of middle and upper SES.<sup>34</sup>

In the United States, England, and Canada, 20%–32% of pregnant women drink, and in some European countries the rate is higher, exceeding 50%. <sup>13–18,36–39</sup> In the Western Cape Province, 34% of urban women and 46%–51% of rural women drink during pregnancy. <sup>40,41</sup> Maternal drinking during pregnancy varies among and within populations throughout the world. <sup>33</sup>

That alcohol abuse and FAS cluster in families implies both social and genetic influ-

ences in susceptibility. 10,42–44 Some alcoholabusing families appear to escape many symptoms of FASD. 7,33,45 Families with 1 or more children with FASD experience serious physical and mental problems that pose a challenge to all types of service providers. 46 Because maternal risk for FASD involves an interaction of biological, familial, historical, social, and psychological factors, 46 research and prevention foci are interdisciplinary. 14

In the general literature on alcohol abuse, maternal risk factors for FASD include smoking; abusing drugs; cohabiting with an alcoholic male partner; sexual dysfunction; having alcohol-abusing parents; initiating drinking at an early age; and having low self-efficacy, poor life goals, and few interests. 3,19,48–55 Protective factors identified as providing strong normative or cultural support for abstinence or light drinking include high education; reli-

giosity; and unique social, psychological, biological, and genetic traits. <sup>9,35,56–58</sup> Nevertheless, many risk factors for FASD are not well understood, and their explication is vital for prevention efforts. <sup>14,59,60</sup>

# **Background of the Region**

We describe a study<sup>9</sup> of maternal risk for FASD in a town and its rural areas (population=45225; 22% of the area is rural) in the Western Cape Province of South Africa. Most inhabitants are "Colored," defined as racially mixed individuals of African, European, and Asian descent. The town is similar to many others in this agricultural and wine-producing region. Heavy, episodic drinking has been the norm among laborers for generations. For several centuries, alcohol was provided daily to farmworkers as partial payment for work, a system known as the "dop" system, after the Afrikaans word for drink. Though this system of payment was formally outlawed by multiple statutes years ago, its effects persist. Local people who are forced to tolerate low pay, limited opportunity, and humble living conditions value alcohol as a favored commodity. Frequent binge drinking, defined as 3 or more drinks per episode of drinking, is common. South Africa researchers have documented high levels of alcohol abuse among male workers of the region. 61-64 Although no formal dop system survives, drinking heavily in groups on weekends and holidays remains a common form of recreation. Commercially produced beer and wine are cheap, readily available, and consumed by a population that, although poor, can allocate enough money to obtain and consume substantial quantities over short periods of time. This pattern results in high BAC values, placing fetuses at risk for  $\bar{\text{FASD}}$ .  $^{65-69}$  We refer to this pattern as the "dop legacy."

Maternal drinking was identified as a serious health problem in Western Cape Province in the mid-1990s.<sup>70,71</sup> Research confirmed high rates of FAS. 8,9,72</sup> We describe risk factors for FAS to improve FAS prevention efforts in this and similar communities.

# METHODS

Beginning in 1999, all children in the Sub-A (first grade) public school classrooms

of the 12 public schools of this area were screened for height, weight, and head circumference. Children at or below the 10th percentile on height and weight and head circumference charts (n=300) were advanced to a second tier of the diagnostic process. Two teams of dysmorphologists, who were blinded to each child's medical history and to one another's findings, conducted a physical examination and measured all features of FAS, recording findings on a quantified dysmorphology checklist in which a high score indicates more FASD features.<sup>8</sup> Ninety-three children who exhibited physical symptoms of FAS that were less consistent or severe were administered psychological and life skills tests<sup>72</sup> to assess development. 19 Next, the biological mothers of these children were located and interviewed about maternal risks. In a formal case conference on each child, findings of all tests/examinations were reviewed, and final diagnoses were made. Sixty-four children were diagnosed with FAS. Maternal interviews were completed for 53 of the 64 mothers of children with FAS who were alive and who could be contacted. These interviews provided the data for our study.

All Sub-A children, with the exception of the 93 children suspected to have FAS, were eligible for selection as control children. One hundred forty-six were selected with a random-number table; their mothers were potential controls. Of these mothers, 30 were not included for the following reasons: 15 (10.3%) mothers could not be located or contacted, the children of 12 (8.2%) mothers were in foster or adoptive placement, and 3 (2.1%) mothers refused participation. The final control sample contained 116 mothers. The development of the children selected as control children was assessed in exactly the same manner as described for case children; none had major anomalies. All mothers were administered identical questionnaires and received incentive gift baskets of food staples.

The questionnaire was developed specifically for the Western Cape Province population by adapting items and techniques from studies in various US ethnic populations. After pilot testing and use with more than 100 women in a previous South Africa study, 9 this version contained 240 items.

Mothers taking the questionnaire were asked to recall behavior and conditions before, during, and after gestation of the index child.

During our study, community residents had little knowledge about FAS and therefore little stigma regarding maternal drinking. Mothers did not know whether their children had FAS at time of interview, because diagnoses had not been finalized. Nevertheless, to establish rapport, nonthreatening questions were asked regarding birth and childhood, occupation, education, diet, reproduction, and general health. Alcohol consumption responses are more accurate in such a format, especially in the context of dietary questions.<sup>73</sup> Respondents were first asked about the drinking habits of their relatives and friends. The context, quantity, and frequency of the mother's current drinking were then explored by means of a 1-week, day-byday log. Drinks were measured in standard ethanol units: 340 mL of beer, 120 mL of wine, or 44 mL of distilled spirits (5%, 11%, and 43% ethanol, respectively). Respondents were shown pictures of standard containers of local brands. Questions on current drinking became benchmarks for reconstructing maternal drinking during pregnancy, and for aiding in memory recall to accurately measure the amount of alcohol consumed, when the alcohol was consumed, and over what duration of time the alcohol was consumed. These questions were asked using the timeline-follow back method, a method that associates drinking with particular events, such as illness, holidays, and celebrations, to pinpoint the amount of drinking that occurred during each stage of pregnancy and during any celebrations or events that occurred while the woman was pregnant.74,75

Smoking was explored more directly, because smoking purchases and practices were more easily remembered and reported, because, unlike drinking, which, in this culture, occurs in groups where drinks are often shared, cigarettes are not shared; an individual must take time from any activities to construct a hand-rolled cigarette for smoking. Respondents were asked about tobacco consumed currently and during pregnancy. One hand-rolled cigarette in South Africa was found in pilot field trials to contain 1 g of tobacco; prerolled cigarettes were rare and

TABLE 1—Demographic, Socioeconomic, and Reproductive Characteristics of Mothers of Children With Fetal Alcohol Syndrome (FAS) (n = 54) and Randomly Selected Control Mothers (n = 116): South Africa, Wave II, 1999–2001

|   | Mothers of Children With FAS | Control Mothers | <u>P (OR)</u>            |
|---|------------------------------|-----------------|--------------------------|
| Age at interview, y, mean (SD)                      | 35.9 (6.3)                   | 34.5 (6.4)      | NSª                      |
| Residence during index pregnancy, %                 |                              |                 |                          |
| Rural   | 66.0                         | 20.9            |                          |
| Urban   | 34.0                         | 79.1            | <.001 <sup>b</sup> (7.36 |
| Educational attainment, y mean (SD)                 | 5.0 (3.2)                    | 8.7 (2.6)       | <.001 <sup>a</sup>       |
| Frequency of church attendance, %                   |                              |                 |                          |
| Never   | 14.3                         | 4.9             |                          |
| Not very often (< 1 times per month)                | 49.0                         | 17.5            |                          |
| Often (1-2 times per month)                         | 14.3                         | 37.9            |                          |
| Very often (1 time per week)                        | 22.4                         | 39.8            | <.001 <sup>b</sup>       |
| Frequency of praying, %                             |                              |                 |                          |
| Never   | 5.6                          | 0.9             |                          |
| Not very often (< 1 time per week)                  | 14.8                         | 9.8             |                          |
| Often (2-3 times per week)                          | 53.7                         | 22.3            |                          |
| Very often (1 time per day)                         | 25.9                         | 67.0            | <.001 <sup>b</sup>       |
| Religiosity index score, c mean (SD)                | 3.0 (0.9)                    | 3.5 (0.7)       | <.001 <sup>a</sup>       |
| Currently employed, %                               | 69.8                         | 66.7            | $NS^b$                   |
| Usual occupation, %                                 |                              |                 |                          |
| Factory worker                                      | 9.6                          | 17.7            |                          |
| Farmworker  | 34.6                         | 12.4            |                          |
| Office worker                                       | 11.5                         | 16.8            |                          |
| Housewife   | 3.8                          | 8.0             |                          |
| Domestic (housekeeper, servant)                     | 15.4                         | 8.8             |                          |
| Other   | 0.0                          | 12.4            |                          |
| Usually does not work                               | 25.0                         | 23.9            | <.003 <sup>b</sup>       |
| Employment status, %                                |                              |                 |                          |
| Full-time   | 42.3                         | 53.2            |                          |
| Part-time   | 11.5                         | 6.3             |                          |
| Seasonal  | 15.4                         | 9.0             |                          |
| Unemployed <sup>d</sup>                             | 30.8                         | 31.5            | NS <sup>b</sup>          |
| Weekly income when working, mean (SD)               | 00.0                         | 02.0            | 110                      |
| Rands   | 105.5 (101.9)                | 252.9 (339.6)   | .002ª                    |
| US\$  | 17.58                        | 42.15           |                          |
| Reproductive variables, mean (SD)                   | 11.00                        | 12.10           |                          |
| Gravidity   | 3.5 (1.4)                    | 2.8 (1.1)       | <.000ª                   |
| Parity, pre- and full term                          | 3.3 (1.4)                    | 2.7 (1.1)       | .002ª                    |
| Miscarriages  | 0.2 (0.5)                    | 0.2 (0.5)       | NS <sup>a</sup>          |
| •   | 0.2 (0.5)                    | 0.2 (0.3)       | NS <sup>a</sup>          |
| Still births  | • •                          | 2.5 (1.0)       | .002ª                    |
| Living children                                     | 3.0 (1.2)                    | 26.1 (6.3)      | .002<br>NS <sup>a</sup>  |
| Age at birth of index child, y                      | 28.0 (6.4)                   | 2.1 (1.2)       | <.001 <sup>a</sup>       |
| Birth order of index child                          | 2.8 (1.4)                    | 2.1 (1.2)       | UU1                      |
| Marital status during pregnancy with index child, % |                              | 40.0            |                          |
| Married   | 29.6                         | 40.9            |                          |
| Unmarried, living with partner                      | 40.7                         | 10.9            |                          |
| Separated/divorced/widowed                          | 1.9                          | 1.8             | - 004h                   |
| Single  | 27.8                         | 46.4            | <.001 <sup>b</sup>       |

Note. NS = nonsignificant. The control group was used as referent.

were counted directly. Questions also assessed other drugs used. Body mass index (BMI) was calculated by means of the following metric formula <sup>76</sup>: weight in kilograms / (height in meters<sup>2</sup>).

Interviews were conducted in Afrikaans, the primary regional language. Over 95% of the participants were Colored; the remainder were Blacks and Whites. We used Epi Info (US Centers for Disease Control and Prevention, Atlanta, GA) for analyses to compare groups with 2-tailed statistical tests (P<.05), and to calculate odds ratios (ORs). Pearson correlation coefficients were used. We compared the characteristics of mothers of children with FAS (case mothers) with the characteristics of randomly selected mothers with normal children (control mothers) from the same schools.

# RESULTS

In this study, 54 of 64 mothers of children with FAS were located alive, and 1 declined an interview (1.9%), yielding 83% participation. After comparing characteristics of the children of the 53 case mothers interviewed with the characteristics of children of the 11 case mothers not interviewed, 1 significant difference was found. The head circumference percentile of children of mothers who were not interviewed was significantly larger (14.9 vs 6.1) than that of children of mothers who were interviewed. Height, weight, verbal and nonverbal ability, behavioral test scores, and dysmorphology scores were not significantly different for FAS children of mothers who were interviewed versus FAS children of mothers who were not interviewed. For the FAS children of mothers who were interviewed versus FAS children of mothers who were not interviewed, there was also 1 difference: dysmorphology scores for children of the interviewed mothers were higher than scores for children of the noninterviewed mothers (2.5 vs 1.4, P = .034). Otherwise, FAS children were similar on all physical and behavioral measures.

As can be seen in Table 1, 3 of the social and demographic variables were not significantly different for case mothers versus control mothers: age at interview, current employment, and full- or part-time employment.

at test.

<sup>&</sup>lt;sup>b</sup>χ<sup>2</sup> test.

Combined values for frequency of church attendance and prayer.

<sup>&</sup>lt;sup>d</sup>Combined categories of unemployed, not employed because of disability, and not employed and not looking for work.

However, case mothers were more likely than control mothers to be rural residents during index pregnancies (OR=7.36), to be employed on farms as their usual occupation (35% vs 12%), and to have lower incomes. Educational attainment of control mothers was 74% higher than that of case mothers (8.7 vs 5 years). Religious practices were scored significantly lower among case mothers (frequency of church attendance, praying, and mean religiosity index).

Case mothers had greater measurements than control mothers for gravidity, parity, living children, birth order of index child, and cohabiting when not married. Miscarriage and stillbirth rates did not differ. The difference in maternal age at birth of case children and control children approached significance (P = .07).

The quantity of alcohol consumed by fathers, mothers, brothers, and sisters of case mothers was significantly greater than for control mothers; fathers of case mothers drank more than fathers of control mothers (Table 2). More than 95% of the fathers of case children drank during the course of the study, consuming a reported 81 drinks per month during the index pregnancies.

There was no difference in the age at which women began drinking (Table 3). However, total past years of drinking at time of interview differed significantly (13.4 years for case mothers vs 3.7 years for control mothers, OR=8.14) and differed nonsignificantly

who were currently drinking at the time of the interview or who had consumed alcohol in the week prior to the interview, were considered (13.4 vs 11.9 years). By the time of interview, 30.2% of case mothers had quit drinking, but a significant difference in current drinking remained between control mothers and case mothers.

Case mothers who drank at the time of the

when control group drinkers (21%), women

interview consumed 15.2 drinks per week (2.8 times the consumption rate for control mothers who drank); 96% binged in the week before the interview. About 90% of all alcohol was consumed on weekends by both groups. The standard for case mothers was much higher than for control mothers (13.1-11.2 drinks/week vs 2.9-4.7 drinks/ week). Of case mothers, 39.6% drank more than the group mean of 12.6 drinks per week, and 24.5% drank 18 or more drinks per week. Only 1.8% of control mothers who drank consumed 12.6 or more drinks per week, and 6.4% consumed 6 or more drinks per week. Because most drinks were consumed on weekends, average daily consumption by case mothers on drinking days was 7.6 drinks if consumption took place over 2 days but 5.1 drinks if consumption took place over 3 days. At the time of interview, average daily consumption of the upper 25% of case mothers was 9.0-24.2 drinks if consumption took place over 2 drinking days and 6.0-16.1 drinks if consumption took place over 3 days.

During pregnancy, case mothers were significantly more likely than control mothers to drink during all trimesters. Case mothers drank at least as much in the months before pregnancy (90.3%) and in all trimesters as they did at the time of the interview.

Beer was the most consumed and favored beverage for both case and control mothers (59% vs 71%), followed by wine (45% vs 20%) and spirits (5% vs 6.5%). Four percent of the case mothers reported having had a problem with alcohol abuse (compared with 2% of the control mothers); 2% of case mothers had received treatment.

Smoking was common among both groups. No significant differences were found in age at which smoking commenced. Current smoking was 66% for case mothers and 30% for control mothers; however, quantity

TABLE 2—Reported Drinking Habits (No. Drinks per Month) of Family and Friends of Mothers of Children With Fetal Alcohol Syndrome (FAS) (n = 54) and Randomly Selected Control Mothers (n = 116): South Africa, Wave II, 1999–2001

|   | Mothers of Children With FAS |                  | Control Mothers |                  | t Test          |                 |
|---|------------------------------|------------------|-----------------|------------------|-----------------|-----------------|
|   | Total<br>Sample              | Drinkers<br>Only | Total<br>Sample | Drinkers<br>Only | Total<br>Sample | Drinker<br>Only |
| Father  |                              |                  |                 |                  |                 |                 |
| No.   | 48                           | 44               | 79              | 55               | <.001           | .012            |
| Mean (SD)                                       | 63.3 (57.1)                  | 69.0 (56.2)      | 31.7 (35.7)     | 45.5 (34.6)      |                 |                 |
| Mother  |                              |                  |                 |                  |                 |                 |
| No.   | 50                           | 31               | 91              | 35               | .027            | NS              |
| Mean (SD)                                       | 28.7 (36.9)                  | 46.2 (37.3)      | 15.7 (30.7)     | 40.7 (38.0)      |                 |                 |
| First brother                                   |                              |                  |                 |                  |                 |                 |
| No.   | 44                           | 39               | 82              | 50               | .034            | NS              |
| Mean (SD)                                       | 51.8 (70.8)                  | 58.4 (72.7)      | 28.8 (48.7)     | 47.2 (55.1)      |                 |                 |
| Second through sixth brothers                   |                              |                  |                 |                  |                 |                 |
| No.   | 31                           | 26               | 37              | 24               | NS              | NS              |
| Mean (SD)                                       | 24.0 (25.7)                  | 33.6 (26.9)      | 22.0 (29.6)     | 36.0 (29.9)      |                 |                 |
| First sister                                    |                              |                  |                 |                  |                 |                 |
| No.   | 37                           | 24               | 69              | 21               | .002            | NS              |
| Mean (SD)                                       | 23.7 (32.8)                  | 36.5 (34.5)      | 7.9 (18.8)      | 26.0 (26.6)      |                 |                 |
| Second through sixth sisters                    |                              |                  |                 |                  |                 |                 |
| No.   | 27                           | 22               | 41              | 15               | NS              | NS              |
| Mean (SD)                                       | 23.0 (20.8)                  | 36.8 (33.7)      | 11.4 (24.9)     | 34.8 (33.2)      |                 |                 |
| Woman's best friend                             |                              |                  |                 |                  |                 |                 |
| No.   | 32                           | 13               | 64              | 13               | .015            | NS              |
| Mean (SD)                                       | 12.3 (24.6)                  | 30.4 (31.1)      | 3.2 (11.7)      | 15.6 (22.5)      |                 |                 |
| Father of index child during<br>index pregnancy |                              |                  |                 |                  |                 |                 |
| No.   | 49                           | 47               | 96              | 70               | <.001           | .002            |
| Mean (SD)                                       | 81.1 (81.7)                  | 84.6 (81.7)      | 34.6 (45.9)     | 47.5 (47.8)      |                 |                 |

Note. NS = nonsignificant.

TABLE 3—Drinking and Smoking Behaviors of Mothers of Children With Fetal Alcohol Syndrome (FAS) (n = 54) and Randomly Selected Control Mothers (n = 116): South Africa, Wave II, 1999-2001

|  | Mothers of Children With FAS |  | Control Mothers           |                           | <i>P</i> (OR)              |                           |
|--|------------------------------|--|---------------------------|---------------------------|----------------------------|---------------------------|
|  | Total Sample<br>(n = 53)     | Drinkers Only <sup>c</sup><br>(n = 35) | Total Sample<br>(n = 109) | Drinkers Only<br>(n = 19) | Total<br>Sample            | Drinkers<br>Only          |
|  | D                            | rinking behavior                       |                           |                           |                            |                           |
| Age first drank alcohol, y, mean (SD)                            | 19.4 (4.5)                   |  | 19.6 (4.6)                |                           | NS <sup>a</sup>            |                           |
| Age began drinking regularly, y, mean (SD)                       | 20.4 (4.3)                   |  | 20.3 (3.7)                |                           | NS <sup>a</sup>            |                           |
| No. years of drinking alcohol, mean (SD)                         | 13.4 (7.3)                   |  | 3.7 (5.7)                 |                           | <.001 <sup>a</sup>         |                           |
| Current drinker, %   | 69.8°                        |  | 21.1                      |                           | <.001 <sup>b</sup> (8.14)  |                           |
| Current alcohol consumption (no. drinks per week), mean (SD)     | 12.6 (13.1)                  | 15.2 (11.2)                            | 1.0 (2.9)                 | 5.4 (4.7)                 | <.001 <sup>a</sup>         | <.001 <sup>a</sup>        |
| Binge drinking (3+ drinks) 1 or more days during past week, %    | 69.6                         | 96.4                                   | 5.5                       | 31.3                      | <.001 <sup>b</sup> (39.31) | <.000 <sup>b</sup> (59.40 |
| Current alcohol consumption on weekends (i.e., Friday, Saturday, | 11.1 (11.1)                  | 13.6 (8.9)                             | 0.9 (2.7)                 | 5.0 (4.2)                 | <.001 <sup>a</sup>         | <.000ª                    |
| Sunday), mean no. drinks (SD)                                    |                              |  |                           |                           |                            |                           |
| Proportion of alcohol consumed during weekends, %                | 88.1                         | 89.5                                   | 90.0                      | 92.6                      |                            |                           |
| Before pregnancy, %  |                              |  |                           |                           |                            |                           |
| Drank about the same (vs current use)                            | 61.5                         |  | 19.4                      |                           |                            |                           |
| Drank less (vs current use)                                      | 1.9                          |  | 2.2                       |                           |                            |                           |
| Drank more (vs current use)                                      | 28.8                         |  | 9.7                       |                           |                            |                           |
| Did not drink  | 7.7                          |  | 67.7                      |                           |                            |                           |
| Stopped during this period                                       | 0.0                          |  | 1.1                       |                           |                            |                           |
| Drank during index pregnancy, %                                  | 92.4 <sup>d</sup>            |  | 19.5                      |                           |                            |                           |
| During first trimester of pregnancy, %                           | <b>5-</b>                    |  |                           |                           |                            |                           |
| Drank about the same (vs current use)                            | 54.7                         |  | 11.7                      |                           |                            |                           |
| Drank less (vs current use)                                      | 5.7                          |  | 3.6                       |                           |                            |                           |
| Drank more (vs current use)                                      | 32.1                         |  | 4.5                       |                           |                            |                           |
| Did not drink  | 7.5                          |  | 78.4                      |                           |                            |                           |
| Stopped during this period                                       | 0.0                          |  | 1.8                       |                           | <.001 <sup>b</sup>         |                           |
| During second trimester of pregnancy, %                          | 0.0                          |  | 1.0                       |                           |                            |                           |
| Drank about the same (vs current use)                            | 52.8                         |  | 8.1                       |                           |                            |                           |
| · · · · · · · · · · · · · · · · · · ·                            | 5.7                          |  | 2.7                       |                           |                            |                           |
| Drank less (vs current use)                                      | 34.0                         |  | 2.7                       |                           |                            |                           |
| Drank more (vs current use)                                      | 7.5                          |  | 80.2                      |                           |                            |                           |
| Did not drink  | 0.0                          |  | 6.3                       |                           | <.001 <sup>b</sup>         |                           |
| Stopped during this period                                       | 0.0                          |  | 0.3                       |                           | <.001                      |                           |
| During third trimester of pregnancy, %                           | E 4 7                        |  | 5.5                       |                           |                            |                           |
| Drank about the same (vs current use)                            | 54.7                         |  | 5.5                       |                           |                            |                           |
| Drank less (vs current use)                                      | 1.9                          |  |                           |                           |                            |                           |
| Drank more (vs current use)                                      | 32.1                         |  | 1.8                       |                           |                            |                           |
| Did not drink  | 7.5                          |  | 85.5                      |                           | <.001 <sup>b</sup>         |                           |
| Stopped during this period                                       | 3.8                          |  | 1.8                       |                           | ~.UU1                      |                           |
| Beverage of choice, % <sup>e</sup>                               | 50.5                         |  | 10.0                      |                           | < 0018 (F.76)              |                           |
| Beer   | 58.5                         |  | 19.6                      |                           | <.001° (5.76)              |                           |
| Wine   | 45.3                         |  | 5.4                       |                           | <.001 <sup>a</sup> (14.62) |                           |
| Spirits  | 5.7                          |  | 1.8                       |                           | NS <sup>a</sup>            |                           |
| Combination  | 1.9                          |  | 0.9                       |                           | NS <sup>a</sup>            |                           |
| Ever had a problem with alcohol abuse, %                         | 4.0                          |  | 1.9                       |                           | NS <sup>b</sup>            |                           |
| Ever received treatment for alcohol abuse, %                     | 1.9                          |  | 0.0                       |                           | NS⁵                        |                           |
|  |                              | Smoking behavior                       |                           |                           | ,a                         |                           |
| Age first used tobacco, y, mean (SD)                             | 18.3 (3.5)                   |  | 18.6 (3.8)                |                           | NS <sup>a</sup>            |                           |
| Age began smoking regularly, y, mean (SD)                        | 18.5 (3.7)                   |  | 19.3 (4.3)                |                           | NSª                        |                           |

Continued

**TABLE 3—Continued** 

| Current smoker, %                            | 66.0        |             | 30.1       |             | <.001 <sup>b</sup> (4.52)  |     |
|--|-------------|-------------|------------|-------------|----------------------------|-----|
| Current tobacco consumption, g/wk, mean (SD) | 27.5 (32.0) | 38.2 (32.4) | 9.3 (17.1) | 27.9 (19.1) | <.001 <sup>a</sup>         | NSª |
| Before pregnancy , %                         |             |             |            |             |                            |     |
| Smoked about the same (vs current use)       | 61.5        |             | 15.7       |             |                            |     |
| Smoked less (vs current use)                 | 7.7         |             | 10.2       |             |                            |     |
| Smoked more (vs current use)                 | 5.8         |             | 3.7        |             |                            |     |
| Did not smoke                                | 25.0        |             | 70.4       |             |                            |     |
| Stopped during this trimester                | 0.0         |             | 0.0        |             | <.001 <sup>b</sup>         |     |
| Smoked during index pregnancy, %             | 75.5        |             | 30.3       |             | <.001 <sup>b</sup> (7.08)  |     |
| During first trimester of pregnancy, %       |             |             |            |             | , ,                        |     |
| Smoked about the same (vs current use)       | 58.5        |             | 14.8       |             |                            |     |
| Smoked less (vs current use)                 | 13.2        |             | 10.2       |             |                            |     |
| Smoked more (vs current use)                 | 5.7         |             | 2.8        |             |                            |     |
| Did not smoke                                | 22.6        |             | 71.3       |             |                            |     |
| Stopped during this trimester                | 0.0         |             | 0.9        |             | <.001 <sup>b</sup>         |     |
| During second trimester of pregnancy, %      |             |             |            |             |                            |     |
| Smoked about the same (vs current use)       | 62.3        |             | 13.5       |             |                            |     |
| Smoked less (vs current use)                 | 9.4         |             | 9.0        |             |                            |     |
| Smoked more (vs current use)                 | 5.7         |             | 3.6        |             |                            |     |
| Did not smoke                                | 22.6        |             | 72.1       |             |                            |     |
| Stopped during this trimester                | 0.0         |             | 1.8        |             | <.001 <sup>b</sup>         |     |
| During third trimester of pregnancy, %       |             |             |            |             |                            |     |
| Smoked about the same (vs current use)       | 64.7        |             | 12.6       |             |                            |     |
| Smoked less (vs current use)                 | 7.8         |             | 9.0        |             |                            |     |
| Smoked more (vs current use)                 | 3.9         |             | 3.6        |             |                            |     |
| Did not smoke                                | 23.5        |             | 73.0       |             |                            |     |
| Stopped during this trimester                | 0.0         |             | 1.8        |             | <.001 <sup>b</sup>         | ,   |
| Current drinker and smoker, %                | 73.6        |             | 11.2       |             | <.001 <sup>b</sup> (22.07) |     |

Note. Sample sizes for drinking behavior were mothers of children with FAS, total sample, n = 53; mothers of children with FAS, drinkers only, n = 35; control mothers, total sample, n = 109; control mothers, drinkers only, n = 19. Sample sizes for smoking behavior were: mothers of children with FAS, total sample, n = 52; mothers of children with FAS, smokers only, n = 34; control mothers, total sample, n = 99; control mothers, smokers only, n = 33.

consumed by smokers in the 2 groups was not significantly different (38 vs 28 g/week). Rural women were more likely than towndwelling women to smoke. Most women "rolled their own," and this practice, along with rural women's low income, tends to limit quantity of use. During pregnancy, 76.5%–77.4% of case mothers smoked. After we combined current drinking and smoking, 73.6% of case mothers reported both smoking and drinking (compared with 11.3% of control mothers).

General physical measurements (Table 4) revealed that case mothers were significantly smaller than control mothers on height, weight, head circumference, and BMI. Head circumference and weight were especially reduced for mothers of FAS children, as indicated by tests of significance. The significant negative correlation coefficients indicate that lower values on the mother's physical measures were associated with higher dysmorphology scores of their children: occipitofrontal circumference

(-.29), weight (-.24), and height (-.23). In other words, the smaller mothers appear to be more likely to produce children with FAS than do the larger mothers.

## DISCUSSION

## Limitations and Strengths of the Study

In a previous maternal risk study in South Africa, 35 of 46 (76%) mothers of children with FAS were located alive (13% had died), and 100% of those who were located agreed

<sup>\*</sup>t test.

<sup>&</sup>lt;sup>b</sup>χ<sup>2</sup> test.

Atthough 37 of the 53 women interviewed reported that they were current drinkers, only 35 had consumed alcohol during the past week. Therefore, the data on current quantity and frequency are based on the responses of the 35 women who reported current drinking.

<sup>&</sup>lt;sup>d</sup>Four women whose children were diagnosed with FAS did not admit to drinking during the index pregnancy. When this inconsistency was revealed during the diagnostic case conferences, these women's children were reassessed. In 2003, 2 dysmorphologists confirmed diagnosis of FAS in each of the 4 cases, as did the doctors evaluating the results of psychological tests. Institute of Medicine criteria allow for a diagnosis of FAS without confirmation of maternal drinking.

<sup>\*</sup>Percentage of beverages reported as favorites and reported as consumed exceeded 100%, because some mothers reported 2 favorites.

TABLE 4—Anthropometric Measures of Mothers of Children With Fetal Alcohol Syndrome (FAS) (n = 54) and Randomly Selected Control Mothers (n = 116): South Africa, Wave II, 1999–2001

| Variable                          | Mean (SD)                       |                    |                |   |  |  |  |
|-----------------------------------|---------------------------------|--------------------|----------------|---|--|--|--|
|                                   | Mothers of<br>Children With FAS | Control<br>Mothers | P <sup>a</sup> | Correlation with Child's<br>Dysmorphology<br>Score (Total Sample) |  |  |  |
| Height, cm                        | 154.3 (6.6)                     | 157.1 (7.6)        | .034           | 23  |  |  |  |
| Weight, kg                        | 59.6 (14.2)                     | 67.9 (15.2)        | .002           | 24  |  |  |  |
| Occipitofrontal circumference, cm | 53.8 (0.8)                      | 54.7 (1.5)         | .001           | 29  |  |  |  |
| Body mass index                   | 24.9 (5.5)                      | 27.4 (5.9)         | .019           | 17  |  |  |  |

at test.

to an interview. Such high numbers located and participating are unparalleled in the FAS literature. However, this study of mothers of confirmed FAS children has limitations. Data were collected retrospectively for the previous 7 years. Accuracy of recall may be a problem despite our efforts to reconstruct accurate patterns from reports of current daily drinking and timeline-follow back methods. The study population also had limited formal education, which may have affected the quality of selfreported alcohol consumption data. Furthermore, the modal drinking pattern was binge drinking, which could have resulted in memory loss. However, retrospective reports of alcohol consumption have been found to be as accurate as<sup>77</sup> or even more accurate than prenatal clinic data, or at least to produce reports of higher drinking levels. 78,79 In addition, recent literature supports the use of day-by-day reporting and reconstruction of drinking histories, 80,81 including details such as BACs. 82 No retrospective methods, however, are believed to be as accurate as daily reporting systems to collect data on drinking outside prenatal settings.80 Maternal drinking during pregnancy is a highly sensitive issue that affects validity. We believe that the questions, sequence, empathic style, and follow-back methods used in our study produced more accurate data (especially for heavy drinking) than have been collected in prenatal settings. 78,79

In 2 waves of research in South Africa, only 1 of 90 mothers of children with FAS contacted has refused an interview. The proportion of women with FAS children not interviewed owing to death, migration, and refusal (20%) has been much lower than in US studies, and candid reporting seems likely in this population thus far. Because all case mothers in our study bore a child with FAS, we describe only the very-highest-risk mothers, as only a few other studies have done. 9,10 This study's detailed data on drinking among mothers of children with FAS are unique. Most studies of maternal drinking during pregnancy are among lower-risk women. Maternal risk is relative and variable between and among populations,58 underscoring the importance of examining control groups from the same population. Risk for FAS births in a single population may not provide accurate measures of generalized or absolute risk (e.g., thresholds). Our findings may be most relevant for comparisons with populations of other developing nations.

## Identified Risk of FAS

All of the women studied belonged to a population of a modernizing society characterized by generally low SES. However, compared with control mothers, case mothers had even fewer social resources, such as education, income, or spirituality. As in other studies, risk for FAS was associated with higher gravidity and parity and thus later-born children. Case mothers were more likely to be unmarried and to live with a male partner and had extended families, sexual partners, and friends who drank heavily. As evidenced from the control group drinking reported in interviews, frequent binge drinking was normative among 50% of men and less than 20% of women. Alcohol consumption was

much greater for case mothers than for control mothers in all comparisons.

Control mothers were more likely to have been abstainers or light drinkers compared with case mothers, who showed significantly heavier drinking patterns and reported drinking at the same level (53%–55%) or higher during pregnancy (32%–34%) compared with current drinking levels. As noted previously, South Africa case mothers often described stressful life events as causes of heavy maternal drinking during pregnancy. A higher risk for FAS clearly exists among those of the lowest SES. See

## Dop Legacy

Most of the alcohol consumed was obtained commercially. Only 5% of the women in this study reported having received alcohol through the dop system (i.e., as payment for labor) in their lifetimes (14% of case mothers vs 1% of control mothers). Of the case mothers, 2% reported having received dop during the index pregnancy, and 0.7% reported having received dop at time of interview. Because of these low rates of actual historical and contemporary contact with the dop system among the study population, the contemporary drinking pattern is better characterized as a dop legacy than as a systematic issuance of alcohol to laborers, as stated in our introduction. Contrary to popular misconception, beer, not wine, is the beverage of choice and abuse.

# Maternal Age, Nutrition, and Anthropomorphic Considerations

In a previous study in this community,9 the mean age of mothers at birth of a child with FAS was low  $(26.7 \pm 7.6 \text{ years})$ ; this age was also relatively low in this sample (28.0  $\pm 6.4$ years). In both studies, the difference between case mothers and control mothers was not significant (P=.07, 2-tailed) despite the larger sample in our study. Maternal age at birth of FAS children was lower than that previously observed in populations in developed countries. 7,25,33 in which a significant difference is always reported between FAS case mothers, case mothers, and control mothers. 10,79 This lack of significance is unique in the literature and is not explained by early age at onset of drinking or drug use in this community.

Rather, it is substantially explained by duration, degree, and regularity of binge drinking during pregnancy, with some other unique cofactors, such as nutrition, body size, and general SES.

Nutrition and maternal body size may partially explain the low maternal age at birth of children with FAS, the high rates of FAS in this population, and the severity of FAS. Poor nutrition (lifelong and current), genetic influences, and multiple generations of fetal alcohol exposure likely contribute to the high rate of FAS. Case mothers were, on average, significantly smaller on all physical measures: height, weight, head circumference, and BMI. Maternal physical traits were negatively associated with their children's dysmorphology scores. Smaller, lighter mothers who engage in binge drinking may be less able to eliminate alcohol via first-pass metabolism, allowing more alcohol to enter the placenta and cause more fetal damage.83 Conversely, heavier mothers have more adipose tissue to which alcohol can be distributed, thereby protecting the fetus. Undernutrition and frequent hunger during pregnancy were reported by more case mothers than control mothers (11.5% vs 4.6%). Finally, the findings of smaller average head circumference among case mothers and of heavier drinking among maternal grandmothers of FAS children raise questions about intergenerational prenatal alcohol exposure and damage. 10 Some mothers of FAS children appear to have FASD themselves; their alcohol abuse may originate in part from behavioral traits associated with FASD (e.g., impulsivity, poor judgment).

## **Protective Factors**

Potential protective mechanisms with preventive implications for this population have been identified. Key protective factors were low gravidity and parity, larger body size, higher educational attainment and income, religiosity, nondrinking male partner, and adequate nutrition.

# Prevention

Public health education on the dangers of maternal binge drinking is needed locally. Prevention is needed in the community, particularly in rural areas. Many risk factors identified are amenable to change via social im-

provement and proven techniques of alcohol treatment and birth control. New treatment and prevention emphasizing outreach in the highest-risk populations of the Western Cape Province can benefit from this research. 13,19 Prevention has been undertaken by health officials of Western Cape Province, but more resources for these efforts are needed. Despite efforts to establish initiatives in FAS prevention,84 more awareness and activity are needed. Impediments to FAS prevention in South Africa are similar to those in the United States: salaries for full-time workers are lacking, and committed individuals cannot effectively transfer time and energy from other commitments to sustain FAS prevention activities. 12 Integrating alcohol use into prenatal screening85 (with HIV and tuberculosis) could be a partial solution.86 In Western Cape Province, the rates of all 3 of these problems are high, and each affects 4.5%-8% of the population. 87,88 Because our research indicates that FAS is increasing in the study community,31 prevention is needed there and elsewhere in Western Cape Province and South Africa.32

## **About the Authors**

Philip A. May and J. Phillip Gossage are with The University of New Mexico Center on Alcoholism, Substance Abuse and Addictions, Albuquerque. Lesley E. Brooke, Anna-Susan Marais, and Loretta S. Hendricks are with the University of Cape Town and the Foundation for Alcohol Related Research, Cape Town, Republic of South Africa. Cudore L. Snell is with the Department of Social Work, Howard University, Washington, DC. Julie A. Croxford is with the Department of Psychiatry and Behavioral Neurosciences, Wayne State University, Johannesbury, Republic of South Africa. Denis L. Viljoen is with the Department of Human Genetics, Faculty of Health Sciences, University of Witwatersrand, National Health Laboratory Service, and the Foundation for Alcohol Related Research, Johannesbury.

Requests for reprints should be sent to Philip A. May, PhD, The University of New Mexico, Center on Alcoholism, Substance Abuse and Addictions, 2650 Yale Blvd SE, Albuquerque, NM 87106 (e-mail: pmay@unm.edu). This article was accepted May 9, 2004.

## **Contributors**

P.A. May was the principal investigator and epidemiologist of the study and led the writing. J.P. Gossage was the data manager and data analyst for the entire project. L.E. Brooke was the program coordinator of the field research in the target community and oversaw clinical assessment and interviews. C.L. Snell, L.S. Hendricks, and A.S. Marais translated the questionnaire into Afrikaans and, with J. Croxford, completed all of the interviews of case and control mothers. D.L. Viljoen was co-investigator

of the project, overseeing the South African medical, research, and programmatic operations.

#### **Acknowledgments**

This project was funded by the National Institute on Alcohol Abuse and Alcoholism, the National Institutes of Health National Center on Minority Health and Health Disparities, and the Foundation for Alcohol Related Research (grants R01AA09440 and R01AA11685).

Sincere thanks are due to Mayor Herman Baily, the Western Cape Community Town Council, Cecil Driver, and the principals of the 12 elementary schools where the study was initiated. Furthermore, Chris Shaw, Carolyn Tullett, Maggie September, Dickie Naude, and others from the Foundation for Alcohol Related Research, University of Cape Town, and the community contributed greatly to the administration, professionalism, and vital energy of the project. Many individuals from the schools, the public health organizations, and the local community, including farm owners and operators, were indispensable in the research process.

The clinical dysmorphology team consisted of Kenneth Lyons Jones, MD, Denis L. Viljoen, MD, Luther K. Robinson, MD, H. Eugene Hoyme, MD, Nathaniel Khaole, MD, Kwade "Kojo" Asante, MD, Richard Findley, MD, and Barbara Quinton, MD. Psychological testing of children was overseen by Colleen Adnams, MD, and conducted by Andrea Hay and Ansie Kitching. Faye Calhoun, DPA, and Kenneth R. Warren, PhD, of the National Institute on Alcohol Abuse and Alcoholism were responsible for initiating all US collaboration on FAS in South Africa.

## **Human Participant Protection**

Protocols and consent forms used were approved by the University of New Mexico, the National Institutes of Health Office of Protection From Research Risks, the ethics committee of the University of Cape Town, and a local, single-site assurance (oversight) committee. All mothers participating in the study provided active consent to participate, and each mother or legal guardian provided active consent for her child's participation in FAS screening.

### References

- Bingol N, Schuster C, Fuchs M, et al. The influence of socioeconomic factors on the occurrence of fetal alcohol syndrome. Adv Alcohol Subst Abuse. 1987; 6:105–118.
- 2. Day NL, Cottreau CM, Richardson GA. The epidemiology of alcohol, marijuana, and cocaine use among women of childbearing age and pregnant women. *Clin Obstet Gynecol.* 1993;36:232–245.
- 3. Day NL, Robles N, Richardson G, et al. The effects of prenatal alcohol use on the growth of children at three years of age. *Alcohol Clin Exp Res.* 1991;15: 67–71.
- 4. Day NL, Zuo Y, Richardson GA, Goldschmidt L, Larkby CA, Cornelius MD. Prenatal alcohol use and offspring size at 10 years of age. *Alcohol Clin Exp Res.* 1999;23:863–869.
- 5. Ernhart CB, Sokol RJ, Martier S, et al. Alcohol teratogenicity in the human: a detailed assessment of specificity, critical period, and threshold. *Am J Obstet Gynecol.* 1987;156:33–39.
- 6. Sokol RJ, Ager J, Martier S, et al. Significant deter-

- minants of susceptibility to alcohol teratogenicity. Ann N Y Acad Sci. 1986;477:87-102.
- 7. May A, Hymbaugh KJ, Aase JM, Samet JM. Epidemiology of fetal alcohol syndrome among American Indians of the Southwest. *Soc Biol.* 1983;30:374–387.
- 8. May PA, Brooke L, Gossage JP, et al. Epidemiology of fetal alcohol syndrome in a South African community in the Western Cape Province. *Am J Public Health*. 2000;90:1905–1912.
- 9. Viljoen D, Croxford J, Gossage JP, Kodituwakku PW, May PA. Characteristics of mothers of children with fetal alcohol syndrome in the Western Cape Province of South Africa: a case—control study. *J Stud Alcohol.* 2002;63:6–17.
- 10. Kvigne VI., Leonardson GR, Borzelleca J, Brock E, Neff-Smith M, Welty TK. Characteristics of mothers who have children with fetal alcohol syndrome or some characteristics of fetal alcohol syndrome. *J Am Board Fam Pract.* 2003;16:296–303.
- 11. May PA, Hymbaugh KJ. A pilot project on fetal alcohol syndrome among American Indians. *Alcohol Health Res World.* 1982;7:3–9.
- May PA, Hymbaugh KJ. A macro-level fetal alcohol syndrome prevention program for Native Americans and Alaska Natives: description and evaluation. J Stud Alcohol. 1989;50:508–518.
- 13. May PA. A multiple-level, comprehensive approach to the prevention of fetal alcohol syndrome (FAS) and other alcohol-related birth defects (ARBD). *Int. J. Addict.* 1995;30:1549–1602.
- 14. May PA. Research issues in the prevention of fetal alcohol syndrome and alcohol-related birth defects. In: Howard J, Martin S, Mail P, Hilton M, Taylor E, eds. *Women and Alcohol: Issues for Prevention Research.* Bethesda, Md: National Institutes of Health; 1996: 93–131.
- 15. Sokol RKJ, Miller SI, Reed G. Alcohol abuse during pregnancy: an epidemiologic study. *Alcohol Clin Exp Res.* 1980;4:135–145.
- 16. Serdula M, Williamson DF, Kendrick JS, et al. Trends in alcohol consumption by pregnant women: 1985 through 1988. *JAMA*. 1991;265:876–879.
- Waterson EJ, Murray-Lyon IM. Drinking and smoking patterns among women attending an antenatal clinic, II: during pregnancy. *Alcohol Alcohol*. 1989;24: 163–173.
- 18. Godel JC, Pabst HF, Hodges PE, et al. Smoking and caffeine and alcohol intake during pregnancy in a northern population: effect on fetal growth. *Can Med Assoc J.* 1992;147:181–187.
- Stratton K, Howe C, Battaglia F, eds. Fetal Alcohol Syndrome Diagnosis, Epidemiology, Prevention, and Treatment. Washington, DC: National Academy Press; 1996.
- 20. Sokol RJ, Ager J, Matier S, et al. Significant determinants of susceptibility to alcohol teratogenicity. *Ann N Y Acad Sci.* 1986:447:87–102.
- 21. Abel EL, Sokol RJ. Maternal and fetal characteristics affecting alcohol's teratogenicity. *Neurobehav Toxicol Teratol.* 1986;8:329–334.
- 22. Darrow SL, Russell M, Cooper ML, et al. Sociode-mographic correlates of alcohol consumption among African-American and white women. *Women Health*. 1992;18:35–50.

- 23. Abel EL. An update on incidence of FAS: FAS is not an equal opportunity birth defect. *Neurotoxicol Teratol.* 1995;17:437–334.
- 24. Abel EL, Hannigan JH. Maternal risk factors in fetal alcohol syndrome: provocative and permissive influences. *Neurotoxicol Teratol.* 1995;17:445–465.
- 25. Jacobson JL, Jacobson SW, Sokol RJ. Increased vulnerability to alcohol-related birth defects in the offspring of mothers over 30. *Alcohol Clin Exp Res.* 1996; 20:356–363.
- 26. Kodituwakku PW, Kalberg W, May PA. The effects of prenatal alcohol exposure on executive functioning. *Alcohol Res Health*. 2001;25:192–198.
- 27. Mattson SN, Goodman AM, Caine C, Delis DC, Riley EP. Executive functioning in children with heavy prenatal alcohol exposure. *Alcohol Clin Exp Res.* 1999; 23:1808–1815.
- 28. Mattson SN, Riley EP. Implicit and explicit memory functioning in children with heavy prenatal alcohol exposure. *J Int Neuropsychol Soc.* 1999;5:462–471.
- 29. May PA, Gossage JP. Estimating the prevalence of fetal alcohol syndrome: a summary. *Alcohol Res Health.* 2001;25:159–167.
- Sampson PD, Streissguth AP, Bookstein FL, Little RE, Clarren SK, Dehane P. Incidence of fetal alcohol syndrome and prevalence of alcohol-related neurodevelopmental disorder. *Teratology.* 1997;56:317–326.
- 31. May P, Gossage J, Brooke L, Croxford J, Viljoen D. An epidemiological analysis of a second wave of data from children with fetal alcohol syndrome and controls in the Western Cape, South Africa [abstract 208]. *Alcohol Clin Exp Res.* 2000;24:41A.
- 32. Viljoen DL, Craig P, Hymbaugh K, Boyle C, Blount S. FAS in South Africa, 2001. MMWR Morb Mortal Wkly Rep. 2003;52:660–662.
- 33. Abel EL. Fetal Alcohol Abuse Syndrome. New York, NY: Plenum Press; 1998.
- 34. Bingol N, Schuster C, Fuchs J, et al. *Adv Alcohol Subst Abuse.* 1987;6:105–118.
- 35. Morse BA, Weiner L. Rehabilitation approaches for fetal alcohol syndrome. In: Spohr HL, Steinhausen HC, eds. *Alcohol, Pregnancy, and the Developing Child.*New York, NY: Cambridge University Press; 1996: 249–268.
- 36: Day NL, Cottreau CM, Richardson GA. The epidemiology of alcohol, marijuana, and cocaine use among women of childbearing age and pregnant women. *Clin Obstet Gynecol.* 1993;36:232–245.
- 37. Centers for Disease Control and Prevention. Alcohol consumption among pregnant and child-bearing aged women: United States, 1991 and 1995. MMWR Morb Mortal Wkly Rep. 1997;46:346–350.
- 38. Bonati M, Fellin G. Changes in smoking and drinking behavior before and during pregnancy in Italian mothers: implications for public health intervention. *Int J Epidemiol.* 1991;20:927–932.
- 39. Primatesta P, DelCorno G, Bonazzi MC, Waters WE. Alcohol and pregnancy: an international comparison. *J Public Health Med.* 1993;15:69–76.
- 40. Croxford JA, Viljoen D. Prospective analysis of alcohol ingestion in 636 pregnant women in rural and urban areas of the Western Cape. Cape Town, South Africa: University of Cape Town, Department of Human Genetics; 1998.

- 41. Croxford J, Viljoen D. Alcohol consumption by pregnant women in the Western Cape. *S Afr Med J*. 1999:89:962–965.
- 42. Kendler KS, Heath AC, Neale MC, et al. A population-based twin study of alcoholism in women. *JAMA*. 1992;268:1877–1882.
- 43. McCaul ME, Turkkan JS, Svikis DS, Bigelow GE. Familial density of alcoholism: effects on psychophysiological responses to ethanol. *Alcohol.* 1991;8:219–222.
- 44. Schuckit MA, Smith TL. An 8-year follow-up of 450 sons of alcoholic and control subjects. *Arch Gen Psychiatry*, 1996;53:202–210.
- 45. Pierog S, Chandavsu O, Wexler I. The fetal alcohol syndrome: some maternal characteristics. *Int J Gymecol Obstet.* 1979;16:412–415.
- 46. Davis A, Lipson A. A challenge in managing a family with fetal alcohol syndrome. *Clin Pediatr.* 1984; 23:304.
- 47. Gomberg ESL. Women and alcohol: use and abuse. *Nerv Ment Dis.* 1993;181:211-219.
- 48. Wilsnack SC. Women at high risk for alcohol abuse. *The Counselor*. 1989;7(1):16–17, 29.
- 49. Wilsnack SC, Klassen AD, Schur BE, Wilsnack RW. Predicting onset and chronicity of women's problem drinking: a five-year longitudinal analysis. *Am J Public Health*. 1991;81:305–318.
- 50. Wilsnack SC. Sexuality and women's drinking. *Alcohol Health Res World.* 1991;15:147–150.
- 51. Wilsnack SC, Beckman LJ. Alcohol Problems in Women: Antecedents, Consequences, and Intervention. New York: Guilford Press; 1984.
- 52. Shore ER, Batt S. Contextual factors related to the drinking behaviors of American business and professional women. *Br J Addict*. 1991;86:171–176.
- 53. Shore ER, Pieri SA. Drinking behaviors of women in four occupational groups. *Women Health.* 1992;19: 55–64.
- 54. Schlesinger S, Susman M, Koenigsberg J. Self-esteem and purpose of life: a comparative study of women alcoholics. *J Alcohol Drug Educ.* 1990;36:127–141.
- 55. Baily S. Women with alcohol problems: a psychosocial perspective. *Drug Alcohol Rev.* 1990;9:125–131.
- 56. Blume SB. Chemical dependence in women: important issues. *Am J Drug Alcohol Abuse.* 1990;16: 297–307.
- 57. Viljoen DL, Carr LG, Foroud TM, Brooke L, Ramsay M, Li TK. Alcohol dehydrogenase-2\*2 allele is associated with decreased prevalence of fetal alcohol syndrome in the mixed-ancestry population of the Western Cape Province, South Africa. *Alcohol Clin Exp Res.* 2001;25:1719–1722.
- 58. May PA, Gossage JP, White-Country M, et al. Alcohol consumption and other maternal risk factors for fetal alcohol syndrome among three distinct samples of women before, during, and after pregnancy: the risk is relative. *Am J Med Gen.* 2004;127C:10–20.
- Hanna EZ, Faden VB, Harford TC. Marriage: does it protect young women from alcoholism? J Subst Abuse. 1993;5:1–14.
- 60. Schimidt C, Klee L, Ames G. Review and analysis of literature on indicators of women's drinking problems. *Br J Addict.* 1990;85:179–192.
- 61. London L, Meyer J, Well V, Taylor T, Thompson MR,

- Mibuli S. An Investigation into the Neurological and Neurobehavioral Effects of Long-Term Agrochemical Exposure and Deciduous Fruit Farm Workers in the Western Cape, South Africa [masters thesis]. Cape Town, South Africa: University of Cape Town; 1995.
- 62. London L. Alcohol consumption amongst South African farm workers: a challenge for post-apartheid health sector transformation. *Drug Alcohol Depend.* 2000;59:199–206.
- 63. Crome IB, Glass Y. The Dop system: a manifestation of social exclusion. A personal commentary on "alcohol consumption amongst South African workers: a post-apartheid challenge, by L. London 1999." *Drug Alcohol Depend.* 2000;59:207–208.
- 64. Parry CDH, Bennetts AL. Alcohol Policy and Public Health in South Africa. New York, NY: Oxford University Press; 1998.
- 65. Pascoe JM, Kokotailo PK, Broekhuizen FF. Correlates of multigravida women's binge drinking during pregnancy: a longitudinal study. *Arch Pediatr Adolesc Med.* 1995;149:1325–1329.
- Maier SE, West JR. Drinking patterns and alcoholrelated birth defects. *Alcohol Res Health*. 2001;25: 168–174.
- 67. Pierce DR, West JR. Blood alcohol concentration: a critical factor for producing fetal alcohol syndrome. *Alcohol.* 1986;3:269–272.
- 68. Goodlett CR, Horn K. Mechanisms of alcoholinduced damage to the developing nervous system. *Alcohol Res Health*. 2001:25:175–184.
- 69. Mattson SN, Schoenfeld AM, Riley EP. Teratogenic effects of alcohol on brain and behavior. *Alcohol Res Health*. 2001;25:185–191.
- 70. Parry CDH. Alcohol problems in developing countries: challenges for the new millennium. *Suchtmedizin in Forschung und Praxis*. 2000;2:216–220.
- 71. Meyers B, Parry CH. Alcohol use in South Africa, 2001: Fact Sheet 6. Tygerberg, South Africa: Medical Research Council of South Africa.
- 72. Adnams CM, Kodituwakku P, Hay A, Molteno CD, Viljoen D, May PA. Patterns of cognitive-motor development in children with fetal alcohol syndrome from a community in South Africa. *Alcohol Clin Exp Res.* 2001;25:557–562.
- 73. King AC. Enhancing the self-report of alcohol consumption in the community: two questionnaire formats. *Am J Public Health.* 1994;84:294–296.
- 74. Sobell LC, Sobell MB, Leo GI, et al. Reliability of a timeline method: assessing normal drinkers' reports of recent drinking and a comparative evaluation across several populations. *Br J Addict.* 1988;83:393–402.
- 75. Sobell LC, Agrwal S, Annis H, et al. Cross-cultural evaluation of two drinking assessment instruments: alcohol timeline followback and inventory of drinking situations. *Subst Use Misuse*. 2001;36:313–331.
- 76. Molarius A, Seidell JC, Sans S, Tuomilehto J, Kuulasmaa K. Educational level, relative body weight, and changes in their association over 10 years: an international perspective from the WHO MONICA Project. *Am J Public Health.* 2000;90:1260–1268.
- 77. Robles N, Day NL. Recall of alcohol consumption during pregnancy. *J Stud Alcohol*. 1990;51:403–407.
- 78. Czarnecki DM, Russell M, Cooper ML, et al. Five-

- year reliability of self-reported alcohol consumption. J Stud Alcohol. 1990;51:68-76.
- Jacobson JL, Jacobson SW, Sokol RJ. Increased vulnerability to alcohol-related birth defects in the offspring of mothers over 30. Alcohol Clin Exp Res. 1996; 20:359–363.
- 80. Searles JS, Helzer JE, Rose GL, et al. Concurrent and retrospective reports of alcohol consumption across 30, 90, and 366 days: interactive voice response compared with the timeline follow back. *J Stud Alcohol.* 2002;63:352–362.
- 81. Gruenewald PJ, Russell M, Light J, et al. One drink to a lifetime of drinking: temporal structures of drinking patterns. *Alcohol Clin Exp Res.* 2002;26: 916–925.
- 82. Carey KB, Hustad JTP. Are retrospectively reconstructed blood alcohol concentrations accurate? Preliminary results from a field study. *J Stud Alcohol.* 2002; 63:762–766.
- 83. Khaole NK, Li TK. Protective alcohol dehydrogenase genotypes for FAS and blood alcohol profiles among mothers of FAS children. Paper presented at: the Annual Meeting of the Research Society on Alcoholism, June 24–29, 2000, Denver, Colo.
- 84. Fetal Alcohol Syndrome: South Africa. A Progress Report on the 1997 Pilot Study, Information Exchange, and Prevention Workshops. Rockville, Md: National Institute on Alcohol Abuse and Alcoholism; 1998.
- 85. Bad Heart Bull LB, Kvigne VL, Leonardson GL, Lacuia L, Welty TK. Validation of a self-administered questionnaire for prenatal alcohol use in Northern Plains Indian women. *Am J Prevent Med.* 1999;16: 240–243.
- 86. Li C, Olsen Y, Kvigne V, Welty T. Implementation of substance use screening in prenatal clinics. *S D J Med.* 1999:52:59–64.
- 87. Groenewald P. Annual Report 2000: Boland Overberg Region. Worcester, South Africa: Dept of Information Management; 2002.
- 88. Republic of South Africa, Western Cape Province. Health Status Report. Cape Town, South Africa: Western Cape Department of Health; 2001.

Copyright of American Journal of Public Health is the property of American Public Health Association and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.