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An Update on Incidence of FAS: FAS Is Not an Equal Opportunity Birth Defect

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ABEL, E. L. *An update on general incidence of FAS: FAS is not an equal opportunity birth defect.* NEUROTOXICOL TERATOL **17**(4) 437–443, 1995.—The incidence of Fetal Alcohol Syndrome is now estimated at 0.97 cases per 1,000 live births in the general obstetric population and 4.3% among "heavy" drinkers. The general incidence is more than 20 times higher in the United States (1.95 per 1,000) compared to Europe and other countries (0.08 per 1,000). Within the United States, the incidence at sites characterized by low socioeconomic status, and African American or Native American background are about 10 times higher (2.29 cases per 1,000) compared to sites with a predominant middle/upper SES and Caucasian background (0.26 per 1,000). Based on racial background, the number of pregnant women in the U.S. giving birth to FAS children is 2,043 per year; if based on socioeconomic status, the number is slightly higher 2,366. Although race and SES are confounded in the U.S. studies, an examination of U.S. and European studies suggests that the major factor associated with FAS is low SES rather than racial background.

Fetal Alcohol Syndrome Incidence Socioeconomic status Race

INTRODUCTION

IN a previous survey (7), the incidence of Fetal Alcohol Syndrome (FAS) in the Western world was estimated at 0.33 cases per 1,000 live born, with a higher incidence among low SES/African Americans than among middle-high SES/Caucasians. That earlier survey was based on 15 prospective studies of general obstetric populations appearing for prenatal care. Since that analysis, there has been almost a two-fold increase in such studies, allowing for a more up-to-date estimate of the incidence of this anomaly and a clearer perspective of at-risk populations.

In addition to studies of the general population, there are also further data concerning the incidence of FAS among "heavy" drinking women (defined as those consuming an average of 2 or more drinks per day, or 5 to 6 drinks per occasion, or a positive MAST score, or clinical diagnosis for alcohol abuse) (6). These data also shed light on risk factors related to FAS. The purpose of the present communication is to open a dialogue on the risk factors for FAS in light of what appears to be a bias in its occurrence.

INCIDENCE IN GENERAL OBSTETRIC POPULATION

The 29 prospective studies included in the current estimate are shown in Table 1. For studies in which there was no statement concerning the occurrence of FAS, the senior authors were contacted; the information they provided is contained in the Table and appropriately noted.

Based on these studies, the worldwide incidence rate of FAS is now estimated at 0.97 cases per 1,000 live births (95 cases out of 97,576). This estimate, based on about twice as many studies as previous examined, is considerably higher than the previous estimate of 0.33 cases per 1,000 (6). If instead of determining the overall rate per 1,000 (adding all cases of FAS and dividing by the number of total cases), one averages the incidence rate from each study, the estimated incidence is a considerably lower 0.50 per 1,000; the median rate per study is an even lower zero cases of FAS per 1,000, which is also the mode. This discrepancy between the mean and median indicates FAS has not been uniformly encountered in these studies. In other words, FAS appears to occur considerably more often (or less often) at some sites than

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TABLE 1

ESTIMATED INCIDENCE OF FAS PER 1000 BIRTHS BASED ON PROSPECTIVE STUDIES

Study Site (Source)	Study Period	Race and Socioeconomic Status	Sample Size	% of Heavy Drinkers*	Number of FAS Cases	Estimated Incidence per 1000
Australia						
Bell & Lumley, 1989 (13)	1985	Caucasian middle	8,884	0.4%	0	0
Gibson et al.; 1983 (27)	1976–80	Caucasian–middle	7,301	10.8%	0[b]	0
Lumley et al.; 1985 (46)	1981–82	Cross-sectional	14,923	1.0%	0	0
Walpole et al.; 1990 (77)	1982–84	Caucasian middle	605	13.0%	0	0
Canada						
Fried & O'Connell, 1987 (25)	–	Caucasian middle	600	3.1%	0	0
Denmark						
Ogston & Parry, 1992 (52)	–	Caucasian, Cross-sectional	286	3.1%	0	0
France						
Rostand et al.; 1990 (63)	1985–86	–	684	7.6%	2	2.92
Germany						
Ogston & Parry, 1992 (52)	–	Caucasian,Cross-sectional	999	0.6%	0	0
Italy						
Primatesta et al.; 1993 (61)	1986–87	Cross-sectional	1,516	7.0%	0	0
Netherlands						
Verkerk et al.; 1993 (75)	1978–79	–	3,447	9.0%	0[c]	0
Portugal						
Ogston & Parry, 1992 (52)	–	Caucasian, Cross-sectional	430	5.1%	0	0
Spain						
Bolumar et al.; 1994 (15)		Caucasian, Cross-sectional	1004	–	0	0
Ogston & Parry, 1992 (52)		Caucasian, Cross-sectional	866	0.2%	0	0
Ogston & Parry, 1992 (52)		Caucasian, Cross-sectional	793	0.5%	0	0
Sweden						
Larsson, 1983 (39)	–	Caucasian, Low SES	464	3.0%	1	1.43
Larsson et al.; 1983 (40)		Caucasian	669	4.0%	1	2.20
Switzerland						
Fricker et al.; 1985 (24)	–	Caucasian	996		0	0
Halperin et al.; 1985 (29)		Caucasian	541		0[d]	0
United Kingdom						
Wright et al.; 1983 (79)		Caucasian middle	900	4.1%	0[a]	0
Plant, 1985 (59)	1980–83	Caucasian, Low SES	1,008	35.6%	0[e]	0
Waterson & Murray-Lyon, 1989 (78)	1982–83	Cross-sectional	2,226	0.4%	0[f]	0
Primatesta et al.; 1993 (61)	1989–90	Cross-sectional	996	1.0%	0	0
Sulaiman et al.; 1988 (69)	1985–86	Cross-sectional	901	1.0%	0[g]	0
United States						
Boston						
Hingson et al.; 1982 (31)	1977–79	Low/African American (inner city)	1,690	2.7%	1	0.59
Ouellette et al.; 1977 (56)		Low/African American (inner city)	633	9.0%	1**	1.58
Rosett et al.; 1978 (62)		Low	322	13.0%	0	0
Cleveland						
Sokol et al.; 1980 (67)	1973–79	Low/African American (inner city)	12,127	1.7%	5	0.41
Sokol et al.; 1986 (65)	–	Low/African American (inner city)	8,331	7.2%	25	3.00
Denver						
Tennes & Blackard, 1980 (70)	–	Caucasian middle	278	2.0%	0	0
Detroit						
Sokol et al.; 1993 (66)	–	Low/African American (inner city)	14,707	6.0%[h]	57	3.9
Loma Linda						
Kuzma & Sokol, 1982 (38)	1974–79	Caucasian middle	5,093	–	0[i]	0
Pittsburgh						
Day et al.; 1989 (20)	–	Low SES (50% African American)	595	24.0%**	0	0
Cornelius et al.; 1994 (19)	1988–92	Low SES	391	13–19%**	0[j]	0
Seattle						
Hanson et al.; 1978§§ (30)	–	Caucasian middle	1,529	7.0%	2	1.31
Little, 1977 (45)		Caucasian middle	801	9.0%	0	0
Total			97,576		95	

Rate per 1,000 = 0.97; Average Rate per study (based on estimated incidence per 1000) = 0.50; Median Rate per study (based on estimated incidence per 1000) = 0.00; Modal Rate per study = 0.00.

*Defined as average of 2 or more drinks per day, or 5–6 per occasion, or positive MAST, or clinical diagnosis, except as noted elsewhere; **Heavy defined as average ≥ 0.89 drinks/day; [a]Barrison et al.; Adverse effects of alcohol in pregnancy. Br. J. Addict. 80:11-22, 1985.

[b-j] Personal Communication: [b]Gibson; [c]Verkerk; [d]Halperin; [e]Plant; [f]Waterson; [g]Florey; [h]Martier; [i]Sokol; [j]Cornelius

§§ Both cases African American

others. As indicated next, this disparity seems to be largely due to differences in the populations examined at these various sites.

INCIDENCE AMONG HEAVY ALCOHOL USERS

Incidence data for FAS among heavy drinkers are presented in Table 2. The rate of FAS in this population is 4.3% (162 cases out of 3,761), about a 2% decrease from our previous estimate (6). The average incidence rate for FAS in this population, based on averaging the incidence rates in each study, is 4.7% whereas the median rate is 1.1%.

CRITICAL DETERMINANTS IN THE OCCURRENCE OF FAS

Ascertainment

The most critical determinant for the presence of FAS continues to be the country in which the study is conducted (7). In the present survey, the rate in the United States is 1.95 per 1,000 (91 out of 46,497 cases) compared to 0.08 per 1,000 (4 out of 51,079 cases) for other countries.

Differences in the importance attributed to some of the features that go into making a diagnosis can also affect incidence rates (2). If there is a tendency on the part of diagnosticians to base their diagnosis of FAS on some ethnic facial feature, e.g., depressed nasal bridge, epicanthic folds, which is actually a normal variant within a particular ethnic group, the number of cases of FAS where those diagnosticians practice might be higher than elsewhere. For example, depressed nasal bridges and retroverted ears are more common among African American children than Caucasians (55,70), whereas epicanthic folds are more common among Native American, Asian, and Hispanic infants (70). In a prospective study with a largely Caucasian population, the presence of African American children in the alcohol-using group would be more likely to receive a diagnosis of FAS simply because the child would be evaluated against a background of Caucasians. If race-standardized norms are not used, claims of low set ears, short palpebral fissure size, etc., may be artifactual and may thereby contribute to higher incidence rates for a particular ethnic group or a particular study site. For instance, the two FAS cases in all of the White middle-class population studies from the United States were both African American (30). Had these two cases been eliminated as nonrepresentative of the population at that site, the incidence of FAS at populations characterized by white middle SES would be zero per 1,000.

Another example is the native Inuit population in Saskatchewan, Canada, for which there are no growth norms, so estimation of growth retardation is virtually impossible, and the presence of epicanthic folds and a concave depression of the nasal bridge between the eyes is very common. As a result, an aboriginal child with unusual facial features whose mother drank at all during pregnancy "receives a very glib diagnosis of Fetal Alcohol Syndrome by primary care physicians." (Nanson, personal communication). However, the peculiar facial features of the FAS child may be readily identifiable, given training and familiarity with the disorder (5,10,18), so that misattribution is a less likely explanation for the higher incidence rates in prospective studies, where the diagnosis is typically made by a dysmorphologist or other trained investigator.

Due to a greater emphasis on identification and clinical management of high-risk individuals by American clinicians, compared to their European colleagues (58), the former may be more prone to attribute unusual facial features, decreased birth weight and signs of newborn or infant irritability to FAS, but differences in national patterns of clinical care are

TABLE 2

ESTIMATED INCIDENCE OF FAS PER 1,000 LIVE BIRTHS AMONG "HEAVY" DRINKING* WOMEN

Study Site	*n*	Number of FAS Cases	Incidence per 1,000
Australia			
Bell & Lumley, 1989 (13)	38	0	0
Gibson et al, 1983 (27)	79	0	0
Walpole et al.; 1990 (77)	79	0	0
Lumley et al.; 1985 (46)	44	0	0
Boston			
Hingson et al.; 1982 (31)	45	1	22
Ouellette et al.; 1977 (56)	42	1	24
Canada			
Fried & O'Connell, 1987 (25)	21	0	0
Cleveland			
Sokol et al.; 1980 (67)	204	5	25
Sokol et al.; 1986 (65)	600	25	42
Detroit			
Sokol et al.; (1993) (66)	882†	57†	65
Finland			
Halmesmäki, 1988 (28)	85	20	235
Autti-Rämö et al.; 1992 (12)	82	10	122
France			
Rostand et al.; 1990 (63)	52	2	38
Hungary			
Vitéz et al.; 1984 (76)	301	25	83
Italy			
Primatesta et al.; 1993 (61)	257	0	0
Pittsburgh			
Day et al.; 1989** (20)	64†	0	0
Cornelius et al.; 1994 (19)	16	0	0
	49	0	0
Seattle			
Hanson et al.; 1978 (30)	70	2	29
Sweden			
Aronson, 1984 (9)	26	5	192
Larsson, 1983 (39)	17	1	59
Larsson et al.; 1983 (40)	21	1	48
Olegard et al.; 1979 (53)	21	7	333
Netherlands			
Verkerk et al.; 1993 (75)	274	0	0
United Kingdom			
Plant, 1985 (59)	281	0	0
Primatesta et al.; 1993 (61)	81	0	0
Waterson & Murray-Lyon, 1989 (78)	8	0‡	0
Wright et al.; 1983 (79)	22	0	0
Total	3761	162	
Rate per 1,000			43.1
Average rate per study			47.0
Median rate per study			11.0
Modal rate per study			0.00

*Defined as average of 2 or more drinks per day, or 5-6 per occasion, or positive MAST, or clinical diagnosis, except as noted elsewhere.

**"Heavy" defined as average ≥ 0.89 drinks/day; †Martier, personal communication; ‡Waterson, personal communication.

TABLE 3

NUMBER OF WOMEN (15-44 YEARS) GIVING BIRTH TO FAS CHILDREN IN THE UNITED STATES IN 1992 BASED ON RACIAL DEMOGRAPHICS

Racial Background	Incidence Estimated Per 1,000	No. of Deliveries	No. of FAS Births
Caucasian*	0.26	2,985,734	776
African American*	2.29	553,173	1,267
Native American†	?	39,000	?
Other			
Total			2,043

*Table 104, U.S. Department of Commerce, Bureau of Census (1993) (68); †Table 27, CDC National Center for Health Statatistics (1993) (67).

suggested here only as a speculative reason for the differences between countries in the incidence of FAS.

Heavy Drinking

The twenty-fold difference in incidence between the United States and other countries also does not appear to be due to differences in the number of heavy drinkers at different sites (see Table 1). For example, the rate of heavy drinking in Cleveland was 1.7%; whereas Boston, with a rate of heavy drinking ranging from 2.7% to 13%, had only one case of FAS, and Australia, with a rate of 0.4% to 13.0%, and Scotland with an even higher rate of 35.6% (59), reported no cases.

On the other hand, the criteria used to define heavy and the amount of alcohol in a "drink" in different studies varies widely. For example, heavy drinking is operationally defined as less than 1 drink per day by some investigators (e.g., 20) and as much as 5 or more drinks per day by others (e.g., 26); whereas, consumption of one-and-a-half drinks per day, or 4 to 5 drinks a day is considered "moderate" by some investigators (3). Thus, the concept of "heavy" drinking among some researchers passes for "moderate" drinking by others, and vice versa (3,8). Labeling a pregnant woman a heavy drinker may affect the readiness to identify her child as having FAS (7). Differences in criteria for heavy drinking will also undermine comparisons between studies which rely on the concept of heavy drinking as a standard referent, and is especially troublesome for estimating the incidence of FAS among heavy drinkers.

The concept of heavy drinking also depends on the amount of alcohol in a drink. For example, a standard drink in the United States contains about 13 g of alcohol compared to 8 g in the United Kingdom (3,59). Thus, a standard drink in the U.S. is about 1.6 standard drinks in the United Kingdom. This may be the reason the percentage of heavy drinkers is so high in Scotland (59) whereas the incidence of FAS is so low (59). Even at a consumption rate of 7 drinks per occasion, the total amount of alcohol consumed in Scotland would be 56 g, far short of the 65 g (5 drinks × 13 g per drink) needed to meet the criteria for heavy drinking in the United States. Thus, differences in the alcohol content of a drink make international comparisons as to the relationship between the amount of drinking and FAS, or the relationship between heavy drinking and FAS, very tentative (3). However, within the United States, the differences in incidence rates at different sites, despite comparable rates of heavy drinking, suggest the population characteristics at these sites may be critical for the occurrence of FAS.

Population Characteristics

In the United States, the incidence of FAS at sites serving a primarily Caucasian/middle SES patient population is 0.26 per 1,000 (2 out of 7,701) almost 10 times lower than the 2.29 per 1,000 rate for sites where the majority of subjects is primarily African Americans/low SES (89 out of 38,796 cases). Because race and SES are confounded in these studies, Tables 3 and 4 provide separate estimates for the number of women giving birth to children with FAS each year from the standpoint of racial demographics and socioeconomic status.

Based on total annual births among Caucasians and African Americans in the U.S. for 1992, (73,74), we would expect a minimum of 2,043 new cases of FAS each year in the United States (Table 3). We are still unable to estimate the incidence of FAS among Native Americans due to an absence of prospective studies for this group. The almost ten-fold difference in incidence between the Caucasian and African American population in the United States would be even greater if the two cases noted in one of the Seattle studies (30) were placed in the African American category since both cases were African American, although the study population was predominantly Caucasian.

Table 4 estimates the number of women giving birth to children with FAS on the basis of maternal socioeconomic status, using incomes of $10,000 or less as the criterion for a family of three (74). The 2,366 cases derived by this analysis is almost identical to the estimate based on racial demographics.

A closer examination of study populations, however, suggests that low SES is indeed the critical factor for the occurrence of FAS at most study sites.

For instance, the first FAS case reports by Jones and Smith (34) included Caucasian, African American, and Native American children, all of whom were seen at Harborview Medical Center in Seattle which "serves a low socioeconomic urban population where a number of factors may combine to produce poor fetal and infant performance" (72). Rosett et al. (62) reported that "most of the women interviewed (in their Boston study) were poorly nourished." Bingol et al. (14) found only one case of FAS out of 109 children born to 36 Caucasian upper middle class alcoholics in New York (1%) compared to 54 cases out of 133 (40.5%) African American and Hispanic lower SES alcoholics. All of Iosub et al.'s (32) clinical patients were on public assistance (welfare) and were either Black (African American) or Hispanic (Iosub, personal communication). Sokol et al.'s (65,67) studies in Cleveland included both African Americans and Caucasians, all of whom were charac-

TABLE 4

NUMBER OF WOMEN (15-44 YEARS) GIVING BIRTH TO FAS CHILDREN IN THE UNITED STATES IN 1992 BASED ON SOCIOECONOMIC STATUS

SES	Incidence Estimated Per 1,000	No. of Deliveries	No. of FAS Births
Low*	2.29	712,500	1,632
Middle-high	0.26	2,823,145	734
Total			2,366

* ≤$10,000/year; Table 104, U.S. Department of Commerce, Bureau of Census (1993) (68).

terized by low SES. All of the more than 14,000 patients in Sokol's Detroit sample were African American and low SES. Of the 207 FAS cases seen at the Kinsmen Children's Centre in Saskatchewan, Canada, as of 1994, 178 were Native Americans or Metis (mixed heritage), 20 were Caucasian, and the remainder were of unknown background . . . "the large majority have biological parents with a low SES" (Nanson, personal communication).

In New York, a study which found an alcohol-related increase in spontaneous abortions among women on public assistance could not be replicated when the same investigators studied private patients (36,37).

In other countries where the population is more racially homogenous and predominantly Caucasian, children with FAS are nearly always characterized by low SES. Lemoine's 127 French children born with what is now recognized as FAS (44) were the offspring of "mostly poor" women, all of whom smoked one to two packages of cigarettes per day (Lemoine, personal communication). Similarly, Dehaene et al. (22) found that all of the 45 French FAS cases he observed were born to women of "low socioeconomic status." All of the mothers studied by Manzke and Spreter von Kreudenstein in Germany were Caucasian (49); 14 of these 17 mothers were low SES, and all smoked, as did the two middle and one upper SES mothers (Manzke, personal communication). All of the 151 FAS cases studied by Steinhausen in Switzerland were Caucasian, and the overwhelming majority had less than a high school education (45 out of 63 known cases) (Steinhausen, personal communication). Nine of the ten Caucasian FAS children studied by Autti-Rämö in Finland (12) were born to mothers characterized by low SES and/or smoking; the mothers of the five FAS children studied by Aronson (9) in Göteborg, Sweden, were all smokers. Of the 147 cases studied by Lesure in Reunion (47), "most of the mothers . . . are unusual smokers, most of them all lower social class and very rarely middle social class (Lesure, personal communication). The mothers of 34 FAS children studied by Mena and her coworkers in Chile (51) had unbalanced (diets) and, partly because of their low socioeconomic status, diets deficient in calories and proteins. In Cape Town, South Africa, all of the 14 FAS cases were observed at Somerset Hospital which serves a population of low socioeconomic background (57).

CONCLUSIONS AND IMPLICATIONS

The major determinant for the occurrence of FAS is poverty. FAS is more common among minorities in the inner cities of the United States, not because some minorities are genetically at-risk for FAS but because a high percentage of minority women eke out an existence at incomes below the poverty line (30.4% for African Americans compared to 8.8% for Caucasians) (74). Poverty, not genotype, provides the kind of host environment that exacerbates alcohol's toxic actions (4).

Some of the reasons the incidence rate for any disorder is higher in one study site than another, besides those already mentioned, include a true disparity in incidence between sites, differences in the medical acumen of those making the diagnosis, differences in the criteria used to make the diagnosis (e.g., 76), and differences in diligence searching for cases (11,41).

Although twin studies indicate genotype can be a factor in susceptibility to FAS (17), it is individual differences in genotypes rather than population differences that seem to be involved. This, in turn, suggests that population studies comparing racial genotypes for rates of alcohol metabolism or susceptibilities to alcoholism will be less fruitful in preventing FAS than studies which identify the socioeconomic risk factors contributing to FAS.

Some of these risk factors are well known. For example, low SES and heavy alcohol consumption are both associated with smoking, poor nutrition, poor health, increased stress, and use of other drugs (1,21,23,31,33,48,54,60,62,67,75,79). Whereas none of these individual factors gives rise to FAS themselves, it is possible, if not likely, that they exacerbate the effects of heavy alcohol intake (1,2,4,16,28,35,42,43,50,54, 64,68,71,79,80), resulting in FAS. The mechanisms underlying the occurrence of FAS may be linked to hypoxia, which leads to intrauterine growth retardation, and increased generation of free radicals, which leads to cell damage (4).

The large variations between the means and the medians in the estimated incidences of FAS in the general population and among heavy drinkers suggest there are either major problems in ascertainment, a higher prevalence of heavy drinking among pregnant women in the United States, or that like opportunistic infections, FAS is expressed only at certain sites where the biological defenses of the population are compromised.

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