Risk Factors for Adverse Life Outcomes in Fetal Alcohol Syndrome and Fetal Alcohol Effects

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ABSTRACT. Clinical descriptions of patients with Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Effects (FAE) suggest major problems with adaptive behavior. Five operationally defined adverse outcomes and 18 associated risk/protective factors were examined using a Life History Interview with knowledgeable informants of 415 patients with FAS or FAE (median age 14 years, range 6–51; median IQ 86, range 29–126). Eighty percent of these patients were not raised by their biological mothers. For adolescents and adults, the life span prevalence was 61% for Disrupted School Experiences, 60% for Trouble with the Law, 50% for Confinement (in detention, jail, prison, or a psychiatric or alcohol/drug inpatient setting), 49% for Inappropriate Sexual Behaviors on repeated occasions, and 35% for Alcohol/Drug Problems. The odds of escaping these adverse life outcomes are increased 2- to 4-fold by receiving the diagnosis of FAS or FAE at an earlier age and by being reared in good stable environments. *J Dev Behav Pediatr 25:228–238, 2004.* Index terms: *fetal alcohol syndrome, fetal alcohol effects, risk factors for adverse life outcomes, life span studies, Fetal Alcohol Spectrum Disorders (FASD).*

Since Fetal Alcohol Syndrome (FAS) was described[1,2] and named,[3] enormous progress has been made in verifying that FAS is a birth defect caused by prenatal alcohol exposure and in identifying patients with FAS in many countries where women drink alcohol.[4] Reported incidence rates of 3 per 1000 births[5,6] would result in 12,000 children with FAS born annually in the United States.[7] The first quantitative assessment of physical, cognitive, and behavioral outcomes of a large group of adolescents and adults with FAS and a few without the full syndrome, documented deficits in intellectual, academic, and adaptive living skills.[8] Although a high rate of maladaptive behaviors was noted, that paper made no attempt to understand the etiology of such problems or to evaluate their consequences in a community context. The present study extends this previous work in several directions and examines not only patients with FAS but also a large number with Fetal Alcohol Effects (FAE) who also have heavy prenatal alcohol exposure but do not manifest the full physical features of FAS. The focus of this paper is on the consequences of maladaptive behaviors and on the adverse life outcomes experienced by patients with FAS/FAE. Additionally, we examine some key risk/protective factors, both personal and environmental, that might exacerbate or ameliorate these adverse life outcomes.

Although the teratogenic effects of alcohol and their mechanisms are well-documented,[9] there are almost no studies of the psychosocial milieu into which children with FAS or FAE are born, or of how this might affect their lives at different stages of development. Each person with FAS or FAE has a mother who abused alcohol to some extent. Among the environmental circumstances frequently found in association with prenatal alcohol damage are early maternal death,[8,10] living with an alcoholic parent, child abuse and neglect,[11–12] being removed from the home by authorities, experiencing repetitive periods of foster care and other transient home placements, and being raised by adoptive or foster families. Rearing families are highly variable. They may have no knowledge of the prenatal exposure history, making it difficult to obtain an accurate diagnosis of an alcohol-related problem. Or, they may be the birth families themselves, with a mother who may or may not be in recovery. To date these environmental characteristics have not been quantified and examined in light of their contribution to adverse psychosocial outcomes for the child with FAS or FAE.

The objective of the present study is to examine adverse life outcomes not previously documented in patients with FAS or FAE, and to evaluate the impact of a variety of personal and environmental characteristics that have the potential to alter the nature and level of adverse life outcomes in these patients. We consider five such adverse outcomes: Inappropriate Sexual Behavior (ISB), Disrupted School Experience (DSE), Trouble With the Law (TWL), Confinement (CNF), and Alcohol and Drug Problems (ADP). We examine them in light of ten influential personal and environmental characteristics that we call "risk and protective factors." Three age groups (children, adolescents, and adults) were evaluated to give the study a lifetime perspective.

METHODS

Subjects

This study involves 415 patients enrolled in the Fetal Alcohol Follow-up Study of the University of Washington's Fetal Alcohol and Drug Unit (FADU) who lived in the Pacific Northwest, who were at least 6 years old between August and December 1995, and for whom a consenting informant could be located. Ninety-one otherwise eligible patients were not represented due to unavailability of an informant or to refusals. These 91 did not differ from the 415 in terms of diagnosis, age at diagnosis, ethnicity, IQ, or sex.

Diagnoses were by dysmorphologists associated with the University of Washington (UW)[2–4,13–17] at the time of original enrollment in the Follow-up Study between 1972 and 1995. Fetal Alcohol Syndrome (FAS) was diagnosed when patients had a positive history of maternal alcohol abuse during pregnancy and (1) growth deficiency of prenatal origin (for height and/or weight); (2) a pattern of specific minor anomalies that included a characteristic face (generally defined by short palpebral fissures; midface hypoplasia, smooth and/or long philtrum, and thin upper lip); and (3) Central Nervous System (CNS) manifestations, including microcephaly or history of delayed development,

hyperactivity, attention deficits, learning disabilities, intellectual deficits, or seizures.[8] The term Fetal Alcohol Effects (FAE) was used for individuals who were exposed prenatally to significant amounts of alcohol, were examined by the same dysmorphologists, and had some but not all of the characteristics of FAS.[4,8] Appropriately informed consent was obtained from each subject or guardian at the time of examination and from each informant at the time of interview. The study was approved by the University of Washington Human Subjects Review Board.

Procedures

Data on diagnosis (FAS vs FAE), age at diagnosis, date of birth, and sex were obtained from patient records. Performance data were from standardized tests administered at FADU. Test scores (see Table 1) were derived from age-appropriate IQ, achievement, and adaptive behavior tests, administered with standard procedures at the FADU: Wechsler Intelligence Scale for Children-Revised,[18] Wechsler Adult Intelligence Scale-Revised,[19] the Wide Range Achievement Test-Revised,[20] and the Vineland Adaptive Behavior Scales.[21]

Life History Interview (LHI). The rest of the data were from the LHI administered by telephone between August and December 1995 to informants such as parents or guardians (see below) who had known the patients for many years. Interviewers were "blind" to contents of the patient records including diagnosis and performance on standardized tests. Designed for this study, much of the LHI is analogous to the "current status and history" questions used in clinical settings; it is suitable for subjects at least 6 years old and produces data for both the risk/protective factors and the adverse life outcomes. The LHI is a 36-page structured interview comprising 450 questions about past and current events that is organized to provide a clear visual guide for the interviewer in standardizing queries and facilitating accurate coding. Each administered interview was reviewed collectively by the team and each coded interview reviewed by the project director. Mean administration time was 70 minutes.

Potential Risk and Protective Factors. Our clinical experience and a pilot study review of our clinical research records[22] produced the list of 10 risk/protective factors shown in Table 1, which include both patient characteristics and life experiences. Coding systems were built into the LHI to quantify them.

Specifically, variables described as "percent of life" are intended to be an explicit quantification. For these, the informant was asked to think back over the history of living situations that the patient had experienced and list for the interviewer the inclusive ages during which the patient's living situation was judged to be "stable and nurturing," the patient had "lived with a person who abused alcohol or drugs," or the patient had "not had their basic needs met." For each of these, a computer algorithm calculated the total years that each patient lived with the relevant risk or protective factor and divided by the patient's age (times 100) to determine the percentage of life that the factor was experienced. "Ever a victim of physical or sexual abuse or

Table 1. Potential Risk/Protective Factors, Adverse Life Outcomes, and Test Performance for Patients with Fetal Alcohol Syndrome (FAS) or Fetal Alcohol Effects (FAE): by Three Age Groups

	Age 6–11.9 yr					Age 12–20.9 yr					Age ≥ 21 yr				
	(n)	%	Mean	Med	SD	(n)	%	Mean	Med	SD	(n)	%	Mean	Med	SD
Risk Protective Factors															
Males (vs females)	(162)	56.2				(163)	62.6				(90)	47.8			
FAS diagnosis (vs FAE)	(162)	28.4				(163)	34.4				(90)	58.9			
Age at FAS/FAE diagnosis (years)	(162)		6.5	6.8	2.5	(163)		12.5	13.4	3.9	(90)		19.6	21.1	10.8
Age at Life History Interview (LHI)	(162)		8.8	8.7	1.8	(163)		16.0	15.8	2.4	(90)		28.4	25.7	7.2
Percent of life in stable/nurturing home	(158)		72.6	82.0	26.3	(161)		68.0	75.0	30.9	(86)		62.9	65.5	31.8
Percent of life with person abusing alcohol/drugs	(153)		35.5	33.0	26.2	(156)		32.9	28.0	27.9	(87)		33.0	30.0	26.7
Percent of life basic needs not met	(151)		26.5	23.5	22.0	(159)		21.1	24.0	14.0	(90)		12.5	15.9	6.0
Ever physical, sexual abuse or domestic violence	(157)	61.1				(161)	70.8				(88)	73.9			
Average years per household by age 18	(160)		2.7	2.1	2.1	(162)		3.8	3.0	3.0	(88)		6.3	6.0	4.6
Good Quality Home Scale for ages 8–12 yr	(162)		6.3	9.0	5.3	(161)		9.4	10.0	3.1	(90)		9.2	10.0	3.3
IQ < 70	(138)	13.8				(149)	10.7				(81)	17.3			
Adverse Life Outcomes															
Inappropriate Sexual Behaviors	(161)	39.1				(160)	47.5				(87)	51.7			
Disrupted School Experiences	(161)	14.3				(162)	62.3				(88)	59.1			
Trouble With the Law	(161)	14.3				(162)	61.1				(89)	58.4			
Confinements	(161)	8.1				(161)	46.0				(90)	57.8			
Alcohol/Drug Problems	(162)	0.0				(162)	29.0				(90)	45.6			
Test Performance															
Wechsler IQ	(134)		86.9	88.5	15.8	(145)		88.1	89.0	15.1	(80)		80.7	80.0	15.9
WRAT Reading standard score	(127)		77.7	81.0	18.2	(133)		83.1	86.0	17.7	(77)		82.1	80.0	19.0
WRAT Spelling standard score	(125)		74.7	77.0	18.5	(132)		80.0	80.0	18.1	(77)		81.2	81.0	16.6
WRAT Arithmetic standard score	(126)		74.1	75.0	16.4	(132)		74.6	76.0	18.7	(77)		74.3	74.0	15.0
VABS Communication standard score	(140)		73.3	71.5	15.1	(146)		66.2	63.5	18.1	(72)		57.8	53.0	24.0
VABS Daily Living Skills standard score	(140)		70.7	70.0	16.7	(146)		67.8	67.5	18.1	(72)		74.2	77.5	22.8
VABS Socialization standard score	(140)		71.7	69.0	13.2	(146)		63.3	60.5	16.9	(72)		63.4	61.5	20.5
VABS Adaptive Behavior Composite standard score	(140)		67.2	66.0	13.6	(146)		61.1	59.5	14.9	(72)		61.1	58.5	20.1

Med, median; WRAT, Wide Range Achievement Test; VABS, Vineland Adaptive Behavior Scales.

domestic violence," a dichotomy, was obtained by asking about each of these individually, and counting "yes" if any of the three were affirmed. "Average years per household by age 18" was obtained by asking about each of the different households in which the patient had lived before the age of 18 and dividing the total count by 18 or by the patient's age if under 18 years. The "Good Quality Home scale for age 8 to 12 years" is a list of 12 home qualities selected a priori to be "good" in terms of potential to prevent adverse outcomes in the pre-adolescent years. Possible scores range from "0" to "12." The items are "people tried to help each other; the environment was reasonably normal; there was quite a bit of structure; the days were generally predictable and not frenetic; there was enough to keep [patient] busy; people worked at fairly regular jobs; someone was in trouble with the law; a parent had a serious mental illness; a parent had or was suspected of having FAS or FAE; the family had enough resources to manage ok; the family was actively involved in a church or a religious group like that; and there were specific

household rules and consequences for their enforcement." (Three items are in reverse order for scoring; data on this scale were coded only for patients who were 9 years and older.)

Adverse Life Outcomes. The five adverse life outcomes (Table 1) also derive from the LHI. Criteria include the following: Inappropriate Sexual Behaviors (ISB): "repeated problems" with one or more of the following 10 inappropriate sexual behaviors: making inappropriate sexual advances, inappropriate sexual touching, promiscuous sexual behavior, exposing behavior, compulsive sexual behavior, voyeuristic behavior (i.e., peeping), masturbating in public, in trouble for incest behavior, making obscene phone calls, having sex with animals, or any other unusual or worrisome sexual behavior; or ever having been in trouble with the law for a sexual offense even once; Disrupted School Experience (DSE): ever suspended, expelled, or dropped out; Trouble With the Law (TWL): ever charged, arrested, convicted, or otherwise in trouble with the law; Confinement (CNF): ever in juvenile detention, jail, prison,

psychiatric hospital, or in inpatient alcohol/drug treatment; Alcohol/Drug Problems (ADP): ever had alcohol or drug problems or received treatment for alcohol, drugs, or both.

Analysis

Odds ratios were calculated for the 9 risk factors as binary variables individually across the five life outcomes (Table 2) for the subsample of subjects aged 12 years and older (n = 253). The quantity tabulated is the ratio of the odds of adverse life outcomes in the subgroup with the factor (or falling above some level of the factor) to the odds of adverse life outcomes in the subgroup lacking the factor. For the purpose of computing odds ratios, factors that are continuous, other than age, were made dichotomous by dividing the distribution at the median. Approximate 95% confidence intervals for these odds ratios were computed by transforming conventional (symmetric) intervals for log odds ratios.

In order to examine the multiple risk factors jointly (and without simplifying to binary categorizations as in the median scores in Table 2) we carried out a number of logistic regression analyses (Table 3). These analyses examine the odds of adverse life outcomes as functions of the environmental and diagnostic risk factors listed in Table 2, including sex. As the nature and prevalence of adverse outcomes is fundamentally different for children, the models of Table 3 address only the patients who are 12 years and older, as does Table 2. These models were built using stepwise procedures for "generalized additive models" as implemented in the S-PLUS statistical analysis system.[23,24] The effects of "Average years per household," age of the patient at diagnosis, and the age of the patient at the time of the LHI were all represented by nonlinear effects in the regression models, the latter two predictors jointly in a single two-dimensional nonlinear surface. To facilitate interpretation, Table 3 reports model-based odds ratios for selected values of the risk/protective factors. The Appendix describes the logistic regression analysis procedures in more detail.

RESULTS

Demographics and Clinical Findings

The 415 subjects include 155 patients with FAS and 260 with FAE, 236 males and 179 females. The majority (60%) of the subjects were white, 25% were Native American, 7% black, and 6% Hispanic. The sample included 162 children 6.0 to 11.9 years (median 8.8 years), 163 adolescents 12.0 to 20.9 years (median 16.0 years), and 90 adults 21 to 51 years (median 28.4 years). Respondents included adoptive mothers (33%); foster mothers, biological fathers, or step-mothers (25%); biological mothers (17%); other relatives, or current or former caretakers (20%); spouse or partner (1%); and others (4%). Most respondents (80%) had known the patients for at least half of their lives and 42% had known the patients their entire lives. Almost all respondents felt knowledgeable about the patients' life histories. Questions that respondents could not answer were scored to indicate absence of knowledge.

As a group, the entire sample had a median age of 14 years and a median age of 10 years at diagnosis. Sixty-seven percent had been the victim of physical or sexual abuse or of domestic violence. Their median percent of life in a stable/nurturing home was 75% of their lives; median years per living situation (up through age 18) was 2.7 years (Table 1). Overall, 42% of these patients were reported

Table 2. Unadjusted Odds Ratios of Risk Factors Across Five Adverse Life Outcomes as Binary Variables Among Patients with Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Effects (FAE), 12 Years and Older

Risk Factor	Inappropriate Sexual Behavior	Disrupted School Exp.	Trouble with the Law	Confinements	Alcohol/Drug Problems
Environmental Factors					
Over 12 yrs of age at FAS/FAE diagnosis	2.25 (1.27, 4.00)	3.27 (1.85, 5.78)	2.92 (1.66, 5.15)	3.03 (1.69, 5.41)	4.16 (2.07, 8.36)
"Low" percent of life in stable/nurturing home	3.13 (1.83, 5.36)	3.10 (1.79, 5.37)	2.16 (1.27, 3.69)	2.97 (1.75, 5.04)	2.44 (1.40, 4.26)
"Fewer" years per house-hold by age 18 yrs	2.22 (1.30, 3.81)	2.20 (1.25, 3.87)	2.10 (1.20, 3.66)	2.27 (1.32, 3.89)	2.19 (1.27, 3.78)
IQ ≥ 70	0.75 (0.34, 1.64)	2.43 (1.07, 5.52)	1.99 (0.90, 4.38)	1.69 (0.76, 3.76)	3.72 (1.24, 11.14)
Victim of physical, sexual abuse/domestic violence	4.36 (2.31, 8.24)	1.37 (0.77, 2.44)	2.13 (1.20, 3.78)	2.03 (1.14, 3.62)	2.71 (1.38, 5.30)
"Poor" Quality Home for ages 8–12 years	1.51 (0.88, 2.59)	3.03 (1.65, 5.56)	2.01 (1.14, 3.54)	1.92 (1.12, 3.30)	1.89 (1.09, 3.28)
"High" percent of life with person abusing alc/drugs	1.42 (0.84, 2.39)	1.84 (1.07, 3.14)	1.45 (0.86, 2.45)	1.82 (1.08, 3.06)	2.22 (1.28, 3.86)
"High" percent of life basic needs not met	1.93 (1.14, 3.25)	1.24 (0.73, 2.10)	1.85 (1.09, 3.14)	1.97 (1.17, 3.30)	1.40 (0.81, 2.40)
Personal Characteristics					
Being male	0.93 (0.56, 1.56)	1.92 (1.13, 3.25)	1.84 (1.09, 3.10)	1.83 (1.09, 3.06)	0.85 (0.50, 1.45)
Being FAE	1.48 (0.88, 2.49)	1.92 (1.13, 3.25)	1.97 (1.17, 3.33)	1.55 (0.93, 2.59)	1.80 (1.04, 3.11)

Odds ratios less than 1 = protection, greater than 1 = risk. A 2-tailed log-symmetric 95% confidence interval is to the right of each odds ratio. Lower confidence interval limits above 1.0 correspond to conventional significance levels of $p \le .05$. "Low," "High," "Fewer," and "Poor" refer to above or below the median for this sample.

Table 3. Adjusted Odds Ratios (with approximate *p* values) for Selected Values of Risk Factors in Nonlinear Logistic Regression Models for Five Adverse Life Outcomes Among Patients with Fetal Alcohol Syndrome (FAS) or Fetal Alcohol Effects (FAE), 12 Years and Older

	ISB (n = 240)	DSE (n = 244)	TWL (n = 245)	CNF (n = 248)	ADP (n = 242)
Environmental Factors					
Low percent life in stable/ nurturing home (18% vs 100%)	4.06 (.0006)	4.67 (.0003)	2.69 (.01)	—	4.10 (.001)
Fewer years per household[a] by age 18 yrs (1.2 vs 9 yrs)	—	—	—	7.35 (.001)	—
Victim of physical, sexual abuse/domestic violence	3.37 (.0004)	—	—	—	2.56 (.02)
Age at diagnosis[a]					
(17 vs 9 yr at Age at LHI = 18)	1.28	1.70	1.92	1.81	0.95
(17 vs 9 yr at Age at LHI = 26)	2.07 (.002)	2.58 (.05)	1.48 (.01)	1.46 (.04)	6.69 (.02)
Personal Characteristics					
Being male	1.04 (.89)	2.31 (.005)	2.23 (.005)	2.35 (.004)	1.30 (.43)
Being FAE	1.15 (.66)	1.90 (.04)	2.26 (.009)	1.55 (.17)	3.07 (.002)

ISB, Inappropriate Sexual Behavior; DSE, Disrupted School Experiences; TWL, Trouble With the Law; CNF, Confinement; ADP, Alcohol/Drug Problems; LHI, Life History Interview.
[a]Factor was included as a nonlinear term.
Odds ratios were computed from fitted nonlinear logistic regression models (see Appendix). All models include a component that is a two-dimensional nonlinear function of Age at FAS/FAE Diagnosis and Age at LHI. Points at which to evaluate odds for Age at FAS/FAE Diagnosis were selected as ages of interest. Points at which to evaluate odds for the first two Environmental Factors were taken as 10th and 90th percentiles of observed distributions on these variables. Other Environmental Factors listed in Table 2 did not contribute significantly given the effects of those listed above. We note that there are competing models using alternate environmental factors that fit the data nearly equally as well; the stepwise algorithm selection is sensitive to particulars of the degree of nonlinear smoothing. However, the effects of the diagnostic factors are stable under alternative parameterizations. Approximate *p* values, given in parentheses, use conventional chi-square approximations to changes in the log-likelihood (or "deviance") divided by degrees of freedom. The *p* value for Age at FAS/FAE Diagnosis compares the two-dimensional nonlinear function of Age at Diagnosis and Age at LHI (representing approximately 6 d.f.) and the smaller (but not "nested") model nonlinear function only of Age at LHI (representing approximately 4 d.f.).

to have been in special education; 66% had been in a "resource room"; about 65% had received remedial help in each of reading and arithmetic; 29% had received life skills training; 21% had received occupational or physical therapy; 11% had therapeutic day care; and 7% had "infant stimulation."

IQ scores for patients with Fetal Alcohol Syndrome (FAS) and for those with Fetal Alcohol Effects (FAE) represent a wide range of intellectual abilities from profoundly retarded to above average IQ (Figure 1). There is an 8-point mean IQ discrepancy, with FAS lower than FAE. According to the usual cutoff score for developmental disability services (IQ < 70), only 13% of these patients with FAS/FAE would be served in the absence of other qualifying criteria (Figure 1). Group means are considerably below population norms for IQ, achievement, and adaptive behavior tests (Figure 2). Arithmetic and the Vineland Adaptive Behavior Scales (VABS) composite score are the areas of greatest functional deficit for these patients. For Arithmetic, the group means for FAS and FAE are each 2/3 of a normative standard deviation below their own mean IQ; for the Adaptive Behavior Composite, the group means for FAS and for FAE are about 1 to 1.5 normative standard deviations below their own mean IQ score (Figure 2).

Descriptive Data on Adverse Life Outcomes

Inappropriate Sexual Behaviors (ISB) on repeated occasions is the most frequent adverse life outcome across the life span (Figure 3a), increasing slightly with each age

category from 39% in children to 48% in adolescents and 52% in adults. Among children, the most frequently mentioned repeated inappropriate sexual behaviors are exposing (20%) and inappropriate sexual touching (19%). Among adolescents and adults, those most frequently mentioned are promiscuity (26%) and inappropriate sexual advances (18%). Across all ages, there is little difference in the overall prevalence of ISB for males compared to females or for FAS versus FAE. However, promiscuity is
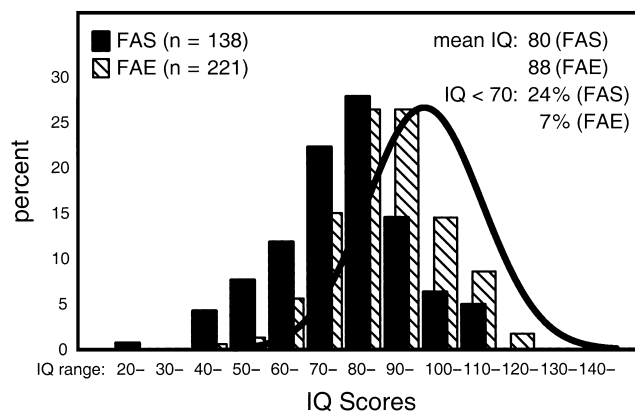
FIGURE 1. IQ Scores of Patients with Fetal Alcohol Syndrome (FAS) and Fetal Alcohol Effects (FAE) superimposed on the normative curve for IQ. An IQ score of 100 is the mean of the population for IQ. The sample size for IQ is below 415 because IQ testing was not funded for this study, but was retrieved from research records as available.
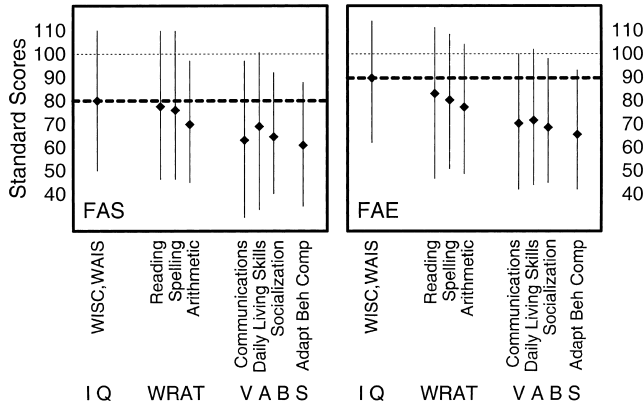
FIGURE 2. Comparison of Standardized IQ, Achievement, and Adaptive Behavior Scores for Patients with Fetal Alcohol Syndrome (FAS) (on the left) and those with Fetal Alcohol Effects (FAE) (on the right). Diamonds represent sample means for each group on each test. Vertical lines connect the 5th and 95th percentile for each group on each test. Bold dashed lines reflect sample IQ means for each group to facilitate comparison with sample means on achievement and adaptive behavior tests for each group. The dotted lines represent the population mean for IQ, achievement, and adaptive behavior tests. Data are from all subjects who have a Wechsler IQ score and additionally have at least one valid Wide Range Achievement Test (WRAT) or Vineland Adaptive Behavior Scale (VABS) score. N = 123 to 138 FAS, and 193 to 221 FAE.

mentioned for twice the fraction of females (22%) as males (11%). Among adolescents and adults, Trouble With the Law (TWL) for ISB was twice as frequent among males (19%) as females (8%).

Disrupted School Experience (DSE) was reported for 14% of school children and 61% of adolescents and adults (Figure 3a). About 53% of the adolescents with FAS/FAE had been suspended from school, 29% had been expelled, and 25% had dropped out. The most frequently mentioned learning problems were attention problems (70%) and repeatedly incomplete schoolwork (58%). The most frequently mentioned behavior problems in school were repeatedly having difficulty getting along with peers (58%) and repeatedly being disruptive in class (55%). The fraction of patients with DSE for whom these problems were mentioned was twice the fraction for the patients without DSE.

Trouble With the Law (TWL) is reported overall for 14% of children and 60% of adolescents and adults (Figure 3a). Among adolescent/adults the most frequently mentioned category of law violations are crimes against persons (45%), which includes shoplifting/theft (36%), assault (17%), burglary (15%), and domestic violence (15%). Among those with TWL, the fraction actually charged, arrested, and/or convicted increases with age from 13% for children to 67% for adolescents and 87% for adults.
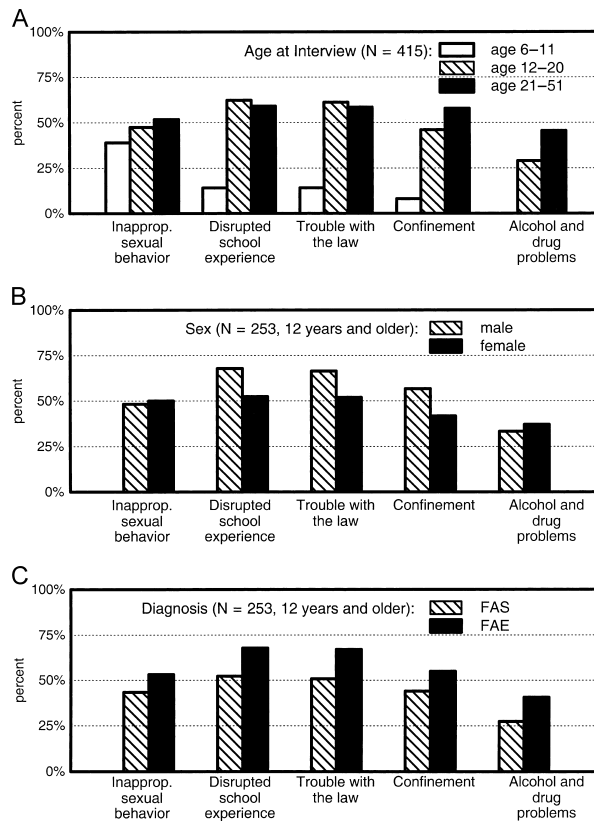

FIGURE 3. Lifespan Prevalence of Five Adverse Life Outcomes: (a) by Three Age Groups, (b) by Male vs Female, and (c) by Fetal Alcohol Syndrome (FAS) vs Fetal Alcohol Effects (FAE). Age group is defined by age at time of Life History Interview (LHI). n = 161 to 162 in the 6- to 11-year-old range, 160 to 163 in the 12- to 20-year-old range, and 87 to 90 in the 21 and older range. For adolescents/adults: n = 141 to 145 males and 106 to 108 females; n = 106 to 109 with FAS and 141 to 144 with FAE.

Confinement (CNF) is reported for 8% of children (all for psychiatric hospitalizations) and 50% of adolescents and adults (Figure 3a). Among adolescents and adults, the fraction reported ever incarcerated for a crime is 35%; ever hospitalized for psychiatric problems, 23%; ever hospitalized for alcohol and drug treatment, 15%.

Alcohol and Drug Problems (ADP) are mentioned for 35% of the patients 12 years and older (29% of the adolescents and 46% of the adults [Figure 3a]). Alcohol problems are mentioned more frequently than are drug problems (33% vs 23%). Almost all of the 57 patients reported to have used street drugs also are reported to have had alcohol problems. Among patients with both problems, alcohol abuse began on average two years before street drug use; 65% of those who abused alcohol went on to use street drugs.

The onset of these adverse outcomes began early for these patients. Problems at school generally began early in their schooling. The mean age of onset of ISBs was 9.6 years; of TWL, 12.8 years; and of ADP, 13.4 years.

Odds Ratios of Risk Factors for Adverse Life Outcomes

In these analyses, the risk factors are treated as binary variables in examining their impact on the five adverse life outcomes in adolescents and adults.

The odds of all five adverse life outcomes are increased 2- to 4-fold for Diagnosis After Age 12 (Table 2). Likewise, odds of all or almost all adverse outcomes are increased with a low percent of life in a Stable/Nurturing Home, fewer Years per Household by age 18, or ever being a Victim of Physical, Sexual Abuse, or Domestic Violence.

Logistic Regression Analysis

In these analyses, the environmental risk factors are treated as continuous (rather then binary) data and, through multiple regression analyses, we are able to adjust one for the other. Personal risk factors (male/female; FAS/FAE) are obviously binary variables.

Results of the logistic regression analyses (Table 3) examine more closely, and generally reinforce, the bivariate relationships depicted in Table 2. As subjects' age at diagnosis and age at the time of the Life History Interview (LHI) are confounded in this study design (the age at LHI being necessarily greater than the age at diagnosis), these analyses model the effects of that pair of age factors jointly. Environmental factors were selected by stepwise regression procedures. As in any multiple regression, the models estimate effects of diagnosis factors adjusting for significant environmental factors, and vice versa. See Appendix for details.

Table 3 shows that environmental factors are clearly important (highly significant) predictors of all five outcomes. For purposes of illustration, Table 3 reports estimated odds ratios pertaining to relatively extreme values (the 10th and 90th percentiles) of the first two quantitative environmental risk factors. However, the *p* values pertain to the *overall* contributions of the risk factors in the logistic regressions; they are not a function of the particular levels

of the risk factors chosen for the computation of the odds ratios in Table 3.

A stable/nurturing home is the most influential protective factor in these analyses, reducing by three- or four-fold the risk of four of the five adverse outcomes examined. In other words, the smaller the percent of life that patients with FAS or FAE spent in stable/nurturing homes, the greater the risk that these patients as adolescents and adults would have more ISB, DSE, ADP, and TWL. Being a victim of sexual, physical abuse or violence also increases the odds for two adverse outcomes (Inappropriate Sexual Behavior and Alcohol/Drug Problems). Years per household was the single significant environmental risk factor for one adverse outcome, namely Confinement.

The nonlinear modeling[23,24] of the effect of age at diagnosis (see Appendix) shows the greatest change in risk roughly over the period from 9 to 17 years, hence our choice of these particular years for computing odds ratios. As the effect of age at diagnosis depends on age at LHI, (which is necessarily greater than the age at diagnosis) we report the estimated odds ratio for an adolescent 18 years old at the time of the LHI and for an adult 26 years old at the LHI.

For an adolescent at 18 years of age, older age at diagnosis (17 vs 9 years) nearly doubles the estimated odds of DSE, TWL, and CNF. For an adult of 26 years of age, older age at diagnosis more than doubles the estimated odds of ISB, DSE, and ADP. (The relatively high odds ratio for ADP for adults is significant but not precisely estimated.)

The coefficients for personal characteristics in Table 3 agree well enough with the simple odds ratios in Table 2. Specifically, "being FAE" and "being male" puts one at higher risk of DSE and TWL. Those with FAE are also at higher risk of ADP while males are also at higher risk of CNF. There is no significant difference between males and females with respect to their risk for ISB and ADP, and there is no difference between FAS and FAE in their risk of ISB and CNF. No interactions were detected between the FAS vs FAE diagnosis factor and any of the other factors in the logistic regression models. Note that IQ < 70 is not in these regressions. That is because it is confounded with FAS in some cases. Note from Table 2 that the effect of IQ is actually protective: the lower the IQ, the better the outcome for 4 of the 5 adverse outcomes.

DISCUSSION

Evaluation of these 415 patients who have either Fetal Alcohol Syndrome (FAS) or Fetal Alcohol Effects (FAE) reveals a lifetime prevalence of adverse life outcomes that documents more specifically the poor prognosis that has been suggested by previous studies.[8,25–29] The understanding that both FAS and FAE are birth defects caused by maternal alcohol abuse, and that 80% of these patients are not raised by their biological mothers, makes it impossible to consider the outcomes of these patients without simultaneously considering their rearing environments. One of the strongest correlates of adverse outcomes is lack of an early diagnosis: the longer the delay in receiving the diagnostic information, the greater the odds of adverse

outcomes. An early diagnosis allows capable caring families to effectively advocate for their children's needs.

Psychological testing of this large group of patients revealed two striking deficits that have been described previously in small samples,[8,30–32] namely specific arithmetic disability and specific problems with adaptive behavior. Although group means for Reading and Spelling are in line with expectations based on mean IQ, the mean Arithmetic standard scores are 2/3 of a standard deviation below mean IQ scores (Figure 2). This finding, which was found for both patients with FAS and those with FAE, suggests a functional deficit in problem solving that should trigger specific interventions. Even more striking is the finding that the mean Adaptive Behavior Composites for FAS and FAE respectively, are far below the normative population mean and 1 and 1.5 normative standard deviations below their respective mean IQ scores (Figure 2). This is a debilitating functional deficit that would probably not be detected in routine IQ testing. This profile suggests a group of patients born with a birth defect who are in apparent need of special services in school and of specialized life skills and job skills training as young adults. As only 24% of those with FAS and 7% of those with FAE have an IQ below 70 (Figure 1) (the traditional qualification for special services), it is clear that these patients will have difficulty getting appropriate services in their schools and in their communities. The 60% rate of Disrupted School Experiences (DSE) among adolescents and adults in this study substantiates what has happened to them historically.

The finding that patients with a diagnosis of FAE, who lack the primary physical stigmata of FAS, nevertheless have clear intellectual, academic, and adaptive behavior deficits, confirms earlier reports [8,33,34] and highlights the particular need for broader recognition and understanding of the full spectrum of fetal alcohol effects. As Figure 3b demonstrates, patients with FAE have higher rates of all five adverse outcomes compared to those with FAS. The finding that having FAE (compared to FAS) doubles the odds of Trouble With the Law (TWL) and Alcohol and Drug Problems (ADP) (Tables 2 and 3) is puzzling until one considers that for many years FAE was thought to be essentially a "nondiagnosis" in contrast to FAS. While beyond the scope of this paper, diagnostic nomenclature is an area in great need of further clarification. This may occur with improved brain/behavior studies such as those now underway[35,36] showing good sensitivity and specificity for detecting patients with both FAS and FAE from age and sex matched controls, and showing comparable deficits in both FAS and FAE.

The only adverse life outcomes we measured that continue to increase into adulthood are Alcohol/Drug Problems (ADP) and Confinement (CNF) (Figure 3a). We identified three strong protective factors against ADP: high percent of life in a Stable/Nurturing Home, younger age at diagnosis, and a diagnosis of FAS (vs FAE) (Table 3). These findings are congruent with clinical experience, where we find that stable, nurturing families with a child diagnosed early, are better able to plan effectively for the transition from adolescence to adulthood, and to maintain as close a relationship with their child in young adulthood as seems necessary. Furthermore, patients with FAS often have

an easier time qualifying for developmental disabilities services and SSI benefits than do those with FAE.

One specific entry in Table 3 is of great societal importance: the contribution of being a victim of physical/sexual abuse and violence to Inappropriate Sexual Behaviors (ISB). Physicians who encounter Inappropriate Sexual Behaviors (ISB) among patients with either FAS or FAE should consider the possibility of victimization. The relation between being a victim of violence and being a subsequent perpetrator of violence is a particularly problematic clinical area in the management of these organically brain-damaged adolescents and adults.

Females and males in this study have comparable rates of Inappropriate Sexual Behaviors (Figure 3b), but the associated consequences may differ, as nearly as we can evaluate them from these data and from our clinical experience. Almost all (50 of 53, or 94%) of the females who had Inappropriate Sexual Behaviors also had experienced sexual, physical abuse or violence against themselves, and 57% of these also had Alcohol/Drug Problems. The types of inappropriate sexual behaviors most often reported for these adolescent and adult females (promiscuity and inappropriate sexual advances) put them at risk of unplanned pregnancies. Thus, Inappropriate Sexual Behaviors, along with the increased odds of Alcohol/Drug Problems, increase the chances of females with either FAS or FAE producing additional alcohol-affected children.[37] In clinical practice, either the child or the mother or both might be fetal alcohol affected and in need of help with family planning as well as other special services.

Males have a higher rate of Disrupted School Experience, Trouble With The Law, and Confinement than do females (Tables 2 and 3), and these three adverse outcomes appear linked. We have complete data on 140 male adolescents and adults: of the 67% who have disrupted school experiences, 83% have been in trouble with the law and, among these, 69% have been incarcerated in jail or prison. In contrast, of the 33% males who have not had Disrupted School Experiences, only 30% have been in Trouble With the Law, and 36% of these have been incarcerated. Support for families advocating to keep adolescents in school and advocating for schools to meet the special needs of these patients, may well be protective against other adverse life outcomes. A recent follow-up study of patients with FAS in Germany, where support services for all disabled children are more comprehensive than those in the United States, found that the patients were not unlike ours in many developmental outcomes but were seldom in trouble with the law.[29]

While these findings have some degree of face validity, caution is always necessary in interpretation. Cause and effect are not clear in cross sectional studies of correlated events. For example, there may be no causality between confinement and household changes (Table 3): being removed from a household and being confined may be competing societal responses to the same undesirable or maladaptive behaviors representing Central Nervous System (CNS) deficits from prenatal alcohol exposure. Fine-grained temporal causality cannot be established by retrospective interviews or multiple regression analyses. The inevitable interactions among the adverse outcomes

themselves also limit interpretation. A person who has dropped out of school is probably more likely to develop alcohol and drug problems and then to get in trouble with the law even in the absence of either FAS or FAE.

Finally, we remind the reader that this is a referred clinical sample, and as such, cannot be considered representative of all people born with FAS or FAE, or even all of those who have a diagnosis of FAS or FAE; this limits the generalizability of the findings. (For example, an adverse life outcome could have been the reason for referral to a diagnostic evaluation in the first place.) Except for those diagnosed at birth whose alcohol exposure history was the trigger for evaluation, there is always the possibility that the manifest problems of the patients brought them to the attention of a diagnostician. Additionally, both the inherent developmental disabilities and the personal characteristics associated with this CNS condition may have contributed to those affected offspring who are brought to a FAS clinic for evaluation. Looking at our data historically, we see that the severely retarded patients were disproportionately diagnosed in the 1970s when the diagnosis was new and before the Surgeon General's (1981) warning on abstaining from alcohol during a pregnancy or when planning a pregnancy.[38] Retarded patients who are already being adequately served in the community may be less likely to be brought in for a diagnostic evaluation now.

Despite the apparent simplicity of Table 2, the family rearing environment for these patients is diverse and multidimensional. Consistent with other studies,[8,39] only 20% of these children were raised by their biological mothers. We found that some mothers achieved sobriety, while others did not. Some achieved sobriety because they had an affected child, others died before knowing their child was affected. Some adoptions occurred at birth, others years later. Some foster families raised children to adulthood without officially adopting them. Other children were in a succession of different households for a variety of reasons, some of which (like behavior problems) stemmed from the child, while others (like aging foster parents) were not child-related. The families, whether biologic, adoptive, or foster, varied widely in both education and finances. To capture and quantify this complexity and richness of life experience, this study demanded an instrument that would produce, on the one hand, a current "snapshot" of each patient's life, and, on the other, a "moving picture" quantifying each patient's unique environmental and personal characteristics from past to present. As we could not find a suitable instrument, we developed our own Life History Interview (LHI). The fact that we did not use a standardized instrument is a limitation in terms of the absence of reliability and validity data, and in terms of replication, but a study of this scope and magnitude could not have been done without it.

While this study has by design focused on adverse outcomes and risk/protective factors in the environment and in the patients themselves, the larger goal of the study is to help families and communities raise the next generation of people born with this birth defect with more understanding, to protect them from the hazardous straits into which they are born, and to provide access to appropriate services so that each can develop to his/her own best potential. This paper suggests that a fetal alcohol diagnosis is important to this goal. We believe that more physicians can play a central role in detecting FAS and FAE and in either making the diagnosis or taking steps to obtain a diagnosis.

We have previously argued that the physician can play an important role in the recognition of FAS among disabled youth and adults.[8] With the work of the past decade, we now propose that the physician be sensitive to the possibility of fetal alcohol problems among children of all ages, as well as youth and adults. We also propose that the physician not just focus on patients with the full FAS, but also be sensitive to the clinical population of patients who are here classified as FAE. They may not display the full clinical characteristics of FAS, yet may have equally heavy prenatal alcohol exposure and be equally impaired. A word on nosology is important here. FAS is characterized by a unique pattern of facial features, growth deficiency of prenatal origin, and some manifestation of central nervous system (CNS) dysfunction. The children here classified as FAE by the dysmorphologists who originally examined them were most usually missing the full facial features and/or the growth deficiency. This paper and others, have demonstrated the importance of examining those suspected of either FAS or FAE, as both may have CNS deficits, and as this paper shows, both may have adverse life outcomes that could presumably be prevented or ameliorated by appropriate interventions. Since these patients were diagnosed, the term FAE is less frequently used. The IOM[7] suggested the term "partial FAS" for patients meeting certain criteria, but also coined the new term "Alcohol-Related Neurodevelopmental Disorders" (ARND) to describe children who had heavy prenatal alcohol exposure along with CNS, neurodevelopmental abnormalities, and/or a complex pattern of behavior or cognitive abnormalities shown through clinical or animal research to be linked to prenatal alcohol. We have found ARND to be a helpful descriptive term in a study of FAS incidence and ARND prevalence.[5] Another classification system developed by Astley and Clarren,[40] the 4-Digit Diagnostic Code, attempts to quantify four primary characteristics (face, growth, CNS, and exposure) according to specific criteria with the idea of developing a consistent "case definition" across clinicians. The system yields a diagnosis of FAS and of static encephalopathy, alcohol exposed. While the two latter systems are attempts at defining specific diagnostic categories, another new term has been coined to allow one to speak of individuals classified by any of these systems as alcohol-affected. The term "Fetal Alcohol Spectrum Disorders" (FASD)[41] is an umbrella term for FAS, FAE, ARND, Partial FAS, and Static Encephalopathy, Alcohol Exposed. The children described in this paper could be called FASD, however, it seemed more accurate to describe them by their original diagnostic nomenclature. While this paper is not about how to diagnose, it clearly points to the value of a diagnosis in ameliorating the postnatal risk factors for adverse life outcomes.

In summary, this study documents the adverse postnatal environments and the corresponding risk of adverse life outcomes among many patients diagnosed FAS or FAE. These include major disruptions in schooling, trouble with the law, inappropriate sexual behaviors, extensive confinements,

and alcohol and drug problems. Adverse life outcomes are not restricted to those with or without the classic facial features of FAS or to those with or without mental retardation. We find that good stable families, with enduring relationships with their children with FAS/FAE, appear to be a critical protective factor for helping children avoid adverse life outcomes.

We also observed a significant reduction in the risk of adverse life outcomes with an earlier diagnosis. We therefore believe that physicians can be important facilitators of improved outcome for patients born with FASD: by systematic querying about maternal alcohol history in patients of any age suspected of alcohol-related disabilities, by making the diagnosis themselves and/or by making appropriate referrals as indicated, by encouraging parents to take an active role in advocating for their children at school and in the community, and by using their experience to improve community supports.

These results suggest that the risk of adverse outcomes might be reduced by families, communities and physicians working together to assure that children with FASD are raised in long-lasting, stable, nurturing homes, and by providing the rearing families with a meaningful diagnosis for their child as early as possible in life.

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APPENDIX

We fitted nonlinear logistic regression models using stepwise model building procedures for "generalized additive models" available in the S-PLUS statistical analysis system.[23,24] These models consider the log odds of adverse life outcomes as possibly nonlinear functions of quantitative risk/protective factors using nonparametric regression procedures, rather than assuming that the log odds are linearly related to a variable such as age of diagnosis (the assumption in conventional logistic regressions). They permit us to identify ranges in the values of a risk/protective factor over which the log odds of an adverse outcome increase or decrease most rapidly, or do not change at all. The degree of smoothness or nonlinearity was specified subjectively. The stepwise model-building algorithm chooses a "best" set of predictors from among those listed in Table 2 on the basis of the common Akaike Information Criterion (AIC). It chooses not only whether to include a predictor, but in the case of quantitative factors, whether to include it as a linear or a nonlinear effect. As this model-building selects from among competing, correlated risk/protective factors on empirical (not theoretical) grounds, the end result should not be considered a "true model" but an analysis useful for assessing the effects of one risk/protective factor adjusting for other competing or confounding variables.

Two of the variables listed in Table 2, age of diagnosis and age at the Life History Interview (LHI), are necessarily strongly correlated in this study design as age at the LHI is greater than or equal to the age at diagnosis. Furthermore, the effects of these two variables should not be considered separately (as one does in the usual "additive" regression model without interaction terms) as the possible effect of age at diagnosis on the log odds of an adverse life outcome will almost certainly depend, to some extent, on the age of the subject at the LHI interview, especially in view of the older adult subjects. We therefore used the "loess" function in S-PLUS to characterize log odds as a general (nonadditive) function of these two age-related variables. For computational reasons, we chose to estimate this joint effect in terms of age at diagnosis and years postdiagnosis (age at LHI minus age at diagnosis).

The joint effect of age at diagnosis and age at the time of the LHI, sex, the indicator of the diagnosis Fetal Alcohol Syndrome (FAS) versus Fetal Alcohol Effects (FAE), and the interaction of these two binary factors (representing 4 sex/diagnosis cohorts) were included in all models. The stepwise regression procedure was used only to determine a "best" set of other environmental measures to include for explanation of the rate of adverse life events. Once a model with environmental effects was selected, we assessed whether the other risk/protective factors played equivalent roles for both FAS and FAE subjects by examining interactions between the FAS/FAE diagnosis indicator and other terms in the model.

The significance of terms in the regression models, reported in Table 3 with p values, was assessed using the conventional chi-squared approximation to the contribution of the term to the fit of the model—the change in log-likelihood or "deviance"—divided by the degrees of freedom for the term. The nonlinear terms in these models (the number of years per household and the joint effects of age at diagnosis and age at the LHI) are represented by non-integer degrees of freedom as explained in Hastie and Tibshirani.[24] To assess the significance of age at diagnosis we compared the model with the joint effect of age at diagnosis and age at LHI with a model including only a (nonlinear) effect of age at LHI.

Finally, in order to facilitate interpretation of the resulting multiple regression models and to compare these with the unadjusted odds ratios in Table 2, we computed model-based odds ratios with respect to selected pairs of values of the risk/protective factors (e.g., to compute an odds ratio comparing patients diagnosed at age 9 with patients diagnosed at age 17).