NCC/IBL aanvraagbon A101014848

Materiaal	Obx	PPN 296996408,854344330 (OCN)	
Titel	Alcoholism: clinical and experimental research		
Deel			
Auteur			
Corporatie	Research Society of Alcoholism		
Jaar/Editie	200X		
Uitgave	Oxford [etc.] Blackwell		
Serie/Sectie			
ISBN/ISSN	1530-0277	ISBN-13	
Plaatscode	854344330 ; MG T 3552 ; rm ; 1990 V14 - 2003 V27		
Jaar	1991-00-00	Datum indienen	29-04-2015 17:14
Volume	15	Datum plaatsing	29-04-2015 17:14
Aflevering	3	Afhandelen voor	
Leenvorm	KOPIE	Datum rappel	13-05-2015
Leveringswijze	E	Aantal rappels	
Coöperatiecode(s)	F	Geplaatst bij	0036/0001
Aanvraagidentificatie		In bezit bij bibliotheek	
Auteur artikel	Abel		
Artikel	Alcoholism: clinical and experimental research		
Bladzijden	514	PPN artikel	
Bron			
Opmerking	UM217555		
Componist			
Artiest			
Bewerker/Samensteller			
Bezetting			
Vorm uitgave			
Moeilijkheidsgraad			
Aanvrager	0036/7001	Bibliotheektype	UKB (U)
Aanvrageridentificatie	MW. S. ROOZEN	Particulier	N
Eindgebruiker	UM217555		
Klant			
Opmerkingen			
Afleveradres post	Mw. S.Roozen Universiteit Maastricht Work & Social Psychologye, Postbus616(UNS40) 6200 MD MAASTRICHT		
E-mail	sylvia.roozen@maastrichtuniversity.nl		
Telefoon			
Opmerking m.b.t. kosten			
		Stuur rekening?	N
Factuuradres	Clearing House		

[1] origineel gestuurd	[4] nog niet aanwezig	[7] uitgeleend
[2] kopie gestuurd	[5] niet aanwezig	[8] wordt niet uitgeleend
[3] overige	[6] niet beschikbaar	[9] bibliografisch onjuist
		[0] bij de binder

Aantal eenheden _____

Aanvraagnummer A101014848

0145-6008/91/1503-0514$3.00/0
ALCOHOLISM: CLINICAL AND EXPERIMENTAL RESEARCH

Vol. 15, No. 3
May/June 1991

A Revised Conservative Estimate of the Incidence of FAS and its Economic Impact

Ernest L. Abel and Robert J. Sokol

We have conducted a new analysis of the incidence of fetal alcohol syndrome (FAS) and its economic impact based on prospectively gathered data of consecutive pregnancies. This more conservative analysis reflects our concern over possible inclusion of "false positives" in our previous estimate and now puts the overall rate in the western world at 0.33 cases per 1000. The estimate among whites is 0.29 per 1000 compared with 0.48 per 1000 for blacks. We did not include estimates for native Americans owing to the absence of prospectively gathered data on FAS for this group. Retrospective studies suggest larger disparities. Both prospective and retrospective studies may be influenced by examiner bias especially for minorities since minorities are often evaluated against standards derived from whites. Based on our estimates and the number of black and white children born each year, we estimate that about 1200 children are born with FAS each year in the United States. This is a probable lower limit based on considerations of ascertainment and absence of relevant information for other minorities such as native Americans. In calculating economic costs, we have now adjusted our estimates to take into account costs that would be incurred whether cases were FAS or not, and also have now included estimated costs for anomalies in FAS cases not considered in previous estimates. Based on these considerations, we now estimate the incremented annual cost of treating this disorder at $74.6 million. About three-quarters of this economic burden is associated with care of FAS cases with mental retardation. This estimate is strictly limited to FAS and not specific alcohol-related birth defects, the prevalence of which is probably much higher. Nevertheless, the extent of the problem and its economic consequences are still substantial.

Key Words: Fetal Alcohol Syndrome, Incidence, Cost Estimates.

FETAL ALCOHOL SYNDROME (FAS) refers to a pattern of anomalies occurring in children born to alcohol-abusing women and includes low birth weight for gestational age or postnatal growth retardation, facial anomalies, and neurological abnormalities.[1,2] The syndrome was first described and labeled in the early 1970s[3] and has become one of the most actively investigated congenital anomalies in the last 2 decades.[4,5] In a previous report, we attempted to estimate the incidence and economic costs associated with FAS in the United States.[6] Since that report, several additional prospective studies have been conducted that suggest that our previous estimates were too high. Our previous estimates may have been inflated because we combined retrospective and prospective studies for our analysis, and retrospective studies tend to be less controlled than prospective studies leading to biased estimates (see below).

One reason retrospective studies may result in erroneous estimates is adoption of the diagnosis-related groups (DRG) system as the basis for payment by health insurers. This system generates possible biases for overdiagnostic coding because it results in greater remuneration.[7] Thus, a FAS diagnosis for a newborn may be entered if the mother is described as being an alcoholic in the medical chart and there is some abnormality such as decreased birth weight, even if there is no specific mention of FAS in the medical record.

At Hutzel Hospital in Detroit, there were 43 cases of FAS listed in the hospital's discharge diagnostic records for the years 1988 to 1989, out of 24,261 live births (Abel, unpublished study). However, examination of the clinical notes indicated that FAS had been specifically diagnosed by a physician for only eight of those 43 cases. Hutzel Hospital is a large teaching hospital with many physicians and basic scientists involved in FAS research. It is a reasonable assumption that recognition of FAS would be less likely a problem at Hutzel than at other sites and when recognized, would be noted in birth charts. Although no specific diagnosis was made, three additional children out of the 43 cases had enough features to satisfy the criteria for FAS. Based solely on the DRG records, the incidence of FAS at Hutzel for 1988 to 1989 was 1.77 per 1000. However, based on physician diagnosis, even with inclusion of the three probable cases the actual incidence would be 0.45 per 1000. (This discrepancy was brought to the attention of the DRG coders and steps have been taken to correct this entry bias).

Another reason prospective studies may result in lower estimates is that women with the greatest risk for FAS may not be included in prospective studies because they do not receive prenatal care and therefore would not be recruited in such studies. For example, in the original reports of FAS by Jones and Smith[3,8] and Jones et al.,[8] four of the 12 women who gave birth to FAS children did not receive any prenatal care. Similarly, Pierog et al.[9] reported that five of the eight mothers of FAS children they examined received no prenatal care, two made visits late in their third trimester, and one made very erratic visits. One woman, the mother of two FAS infants, was not even aware of her pregnancy with her second child

From the Department of Obstetrics and Gynecology, and the Fetal Alcohol Research Center, Wayne State University, Detroit, Michigan.

Received for publication May 2, 1990; accepted December 31, 1990
This study was supported by grant P50 AA07606.

Reprint requests: E. L. Abel, Ph.D., C. S. Mott Center for Human Growth and Development, 275 E. Hancock, Detroit, MI 48201.

until she arrived in the emergency room and was told she was in labor. Thus, retrospective studies may result in higher estimates than prospective studies because they are more inclusive. However, retrospective studies are methodologically less rigorous than prospective studies and estimates derived from such studies may be distorted by factors associated with methodology.

At the time of our initial survey,[6] there were so few prospective studies that we combined retrospective with prospective studies to generate our estimates from a relative larger sample size. The publication of additional prospective studies allowed us to be more restrictive and still rely on a large sample size for our present analysis.

In our previous analysis, we did not take into account different racial susceptibilities for FAS or ethnic population differences for our projections, but instead projected our estimates to the population at large. If some racial groups are at greater risk than others, they might be overly represented if sample estimates are projected to the total population instead of to their respective ethnic populations. The projected number of children born with FAS overall could then be inflated. To minimize this possibility, we have based our projections on the incidence of FAS among various ethnic groups and have based our overall projections on the proportion of these groups in the total population. We are also aware of four surveillance studies that have been published since our initial survey (see Table 1). Although we did not rely on these data for our incidence estimates, we have commented on these studies in the context of ethnic susceptibilities.

Following our revised estimates, we discuss some of the biases in diagnosis that may still result in an inflated estimate of the frequency of FAS. We then proceed to an estimate of FAS economic consequences. In this new analysis, we have also gone beyond our previous effort by adjusting for "background" cases, i.e., cases for which FAS is an additional, but not necessarily causal factor, and include estimated costs for anomalies in FAS cases not considered in our previous estimate.

INCIDENCE

For this current study, we have again confined our estimates to FAS and its associated anomalies rather than the much broader category of alcohol-related birth defects (ARBD). We did this because there are specific criteria for FAS[1,2] whereas it is still difficult to attribute specific anomalies associated with prenatal alcohol exposure unambiguously to alcohol,[10-12] mostly because large numbers of alcohol-abusing mothers are also multiple substance abusers.[11,13] ARBD probably occurs much more frequently than the full syndrome, with substantial medical, social, and economic consequences, magnifying the impact of heavy prenatal alcohol exposure on pregnancy outcome.

In our previous study[6] we estimated the overall incidence of FAS in the western world at 1.9 cases per 1000 live born infants. This estimate did not take into account the way samples were selected at various sites and, as mentioned earlier, included retrospective and prospective studies. Based solely on the prospective studies in which pregnancies were followed consecutively, we now estimate the incidence of FAS in the western world at 0.33 cases per 1000 (See Table 1), which is about six times lower than our previous estimate. Depending on ethnic background and socioeconomic status characteristics of the population studied, the range in rates at these sites varies from 0 to 1.58 per 1000.

This estimate is lower than our findings from our prospective case control study.[14] In that study of 8331 consecutive pregnancies from Cleveland, we identified 600 MAST-positive patients and examined each of their children along with those born to a group of matched MAST-negative women. Out of the 1200 infants examined, there were 25 with FAS, resulting in an incidence of 20.8 per 1000 for this selected group and an incidence of 3.00 for the entire population, about 10 times higher than the minimal estimate presented in this study.

One reason for the higher estimate in the case control study is the closer scrutiny given these patients. In other words, features may have been identified because they were being looked for. Another reason, apart from possible racial/socioeconomic considerations, could be a higher rate of "heavy drinking" among the Cleveland alcohol users compared to those at other sites. [In the Sokol et al.[14] study, there was a relatively high percentage of MAST-positive patients (7.2%)]. However, even allowing for differences in criteria, differences in the prevalence of "heavy" drinking cannot account for differences in FAS estimates reported at various sites (see Table 1). Table 2 summarizes studies reporting the prevalence of heavy drinking among pregnant women at study sites throughout the country. The range in estimates of heavy drinking (0%–9%) in Table 2 is similar to that listed in Table 1. This implies that the rates at the latter are probably accurate or as accurate as our present screening tests permit.

The most critical determinant of incidence rates appears to be the population characteristics of the study site. Most identified cases of FAS in North America still come from sites where the majority of mothers are black or Indian, or where socioeconomic status (SES) is low. Table 1 shows that at study sites in North America where the population was primarily black, the incidence rate, based on prospectively gathered data, was 0.48 per 1000 compared with 0.29 per 1000 where the population was primarily white. Interestingly, the two FAS cases in one Seattle study[27] were both born to the same black mother. The same ethnic preponderance of FAS was reported by Bingol et al.[48] who found only one case (1%) of FAS among a group of 36 white upper middle class chronic alcoholics compared with 40.5% among a group of 48 black and Hispanic lower class alcoholic women. In the Sokol et al.[14] study, 20 of

Table 1. Estimated Incidence of FAS Per 1000 Births

Study site (source)	Study period	Race and socioeconomic status	Type of study*	Sample size	% of Heavy drinkers†	Number of FAS cases	Estimated incidence Per 1000
Australia/New Zealand							
Bell and Lumley[15]	1986	White middle	P	8,884	0.4%	0	0
‡ Gibson et al.[16]	1976–80	White middle	P	7,301	0.6%	0	0
Lumley et al.[17]	1981–82	Cross-sectional	P	14,923	1.0%	0	0
Sweden							
Olegard et al.[18]	1977–78	White	P	7,600		12	1.58
Larsson[19]		White	P	699	13.0%	1	1.43
U.K.							
§ Wright et al.[20]		White middle	P	900	4.1%	0	0
‖ Plant & Plant[21]	1980–83	White middle	P	1,008	2.2%	0	0
¶ Waterson & Murray-Lyon[22]	1982–83	Cross-sectional	P	2,266	1.0%	0	0
Boston							
Hingson et al.[11]	1977–79	Low/black (inner city)	P	1,690	2.7%	1	0.59
** Ouellette et al.[23]		Low/black (inner city)	P	633	9.0%	1	1.58
Cleveland							
Sokol et al.[24]	1973–79	Low/black (inner city)	P	12,127	1.7%	5	0.41
Denver							
Tennes & Blackard[25]		White middle	P	278	2.0%	0	0
Loma Linda							
†† Kuzma & Sokol[26]	1974–79	White middle	P	5,093		0	0
Seattle							
‡‡ Hanson et al.[27]		White middle	P	1,529	7.0%	2	1.31
Little[28]		White middle	P	801	9.0%	0	0
U.S.A.							
Chavez et al.[29]	1981–86	White	S	3,361,963		302	0.09
		Blacks		585,455		340	0.58
		American Indians		19,412		58	2.99
		Hispanics		261,810			0.08
		Asians					0.03
Washington State							
§§ LeMier	1987–88	White	S	116,974		2	0.01
		Black		7,057		1	0.14
		Indian		3,937		0	0
		Other		14,832		0	0
California State							
‖‖ Croen et al.[30]		White		245,938		26	0.11
		Black		39,086		23	0.59
		Hispanic		98,145		4	0.04
		Asians		38,327		0	0.00
		Others		26,761		5	0.19
British Columbia, Canada							
Wong¶¶	1973–80	Cross-sectional (excluding Native Indians)	S	284,331		71	0.25
		Native Indian only	S	9,901		47	4.7

* P, prospective; S, surveillance.

† Heavy drinking is defined as consumption of two or more drinks per day, or five to six drinks per occasion, or clinical judgment of alcohol abuse, or a positive response to a questionnaire such as the MAST.

‡ Gibson, personal communication.

§ Barrison et al.[32]

‖ Plant & Plant, personal communication.

¶ Waterson, personal communication.

** Diagnosed at one year of age.

†† Sokol, unpublished data.

‡‡ Same black mother gave birth to both.

§§ Personal communication, unpublished data.

‖‖ Harris, personal communication.

¶¶ Wong, unpublished study.

the 25 FAS cases were black, although only about half of the study population was black. Although there are no prospective studies in this area focusing on native Americans, two surveillance studies suggest a much higher incidence among these people compared with whites or blacks (see Table 1, cf[49]). In this regard, it is also interesting to note that six of the 11 FAS children originally described by Jones et al.[8] in Seattle were of native American origin.

The significance of these findings as far as incidence is concerned is that racial background/low socioeconomic

Table 2. Incidence of Heavy Drinking (Average of Two or More Drinks Per Day) During Pregnancy in the United States

Study site	Socioeconomic status (SES)	Sample size	% of Heavy drinkers	References
Baltimore	Cross-sectional	624	6.6	Fox et al.[33]
Boston	Lower SES (inner city)	633	9	Ouellette et al.[23]
	Same	1,690	2	Alpert et al.[34]
	White, middle SES	12,440	2.8	Marbury et al.[35]
	Lower SES	1,711	9	Weiner et al.[36]
Buffalo	Cross-sectional	88	8	Russel and Bigler[37]
Calaway County, Missouri	Rural, white, middle SES	255	0	Kruse et al.[38]
California	Middle SES (mainly white)	12,406	3.9	Kuzma and Kissinger[39]
	Middle SES	34,660	0.5	* Mills and Graubard[40]
	Middle SES	32,019	0.4	Harlap and Shiono[41]
Cleveland	Lower SES (inner city)	12,127	1.7	† Sokol et al.[24]
	Lower SES (inner city)	8,331	7.2	† Sokol et al.[14]
Colorado	Middle-low SES	278	2	Tennes and Blackard[25]
Mississippi	Lower SES	428	1.2	Stephens[42]
New York	Cross-sectional	657	1.2	Kline et al.[43]
Philadelphia	Lower SES	326	2.1	Brooten et al.[44]
Seattle	Middle and upper SES	801	9	Little[28]
	Same	1,529	2.9	Streissguth et al.[45]
	Same	156	2	Little et al.[46]
	Same	1,413	0.8	Streissguth et al.[47]

* Three or more drinks per day.
† MAST-positive.

Table 3. Number of Children Born with FAS in the United States in 1987 Based on Racial Demographics

Racial background	Estimated incidence	No. of births in 1987	No. of FAS births
White	0.29 per 1,000	2,992,488	868
Black	0.48 per 1,000	641,567	308
American Indian	? per 1,000	43,707	?
Other		128,631	
		Total	1,176+

status appears to be significantly related to FAS. The explanation for this relationship is anything but straightfoward. Do certain ethnic groups have a genetic susceptibility for FAS? Does low SES predispose to FAS? Is race/socioeconomic status a confounding factor in FAS? Is the difference in incidence between racial groups due to experimenter bias?

ARE MINORITIES AT RISK FOR FAS?

In a previous study, we reported that blacks had a considerably higher risk for FAS than whites.[14] Birth defects monitoring programs, based on large population bases, support this finding. However, such surveillance studies very often underestimate prevalence. Since hospitals voluntarily participate, data are not necessarily representative of the population, the same criteria are not used for diagnosis, and physicians are not equally as skilled

Table 4. Annual Cost Estimates Associated with FAS-Related IUGR

	Total cases	Cases requiring intensive care	Cost for intensive care	Total cost
Initial Cohort	1,176			
Growth retardation at birth				
	844*			
1500–2500 G (LBW)	701†	280‡	$20,000	$ 5,600,000
<1500 G (VLBW)	143§	143‖	$40,000	$ 5,720,000
Re-hospitalization of low birth weight infants				
1500–2500 G (LBW)	644¶	122**	12.5 days @ $372/day	$ 567,300
<1500 G (VLBW)	132¶	50**	16.2 days @ $372/day	$ 301,320
Additional single-year morbidity	(760 cases)††			
	144‡‡		$ 1,405	$ 202,320
Total annual cost				$12,390,940

* 77% of 1,176 FAS cases each year (906) are LBW less 6.8% (62) not uniquely attributable to FAS = 844.
† 83% of 844 cases are LBW = 701.
‡ 40% of 701 LBW cases in intensive care = 280.
§ 17% of 844 (143) cases are VLBW.
‖ 100% of 143 VLBW cases require intensive care = 143.
¶ IOM estimated 8% mortality of 701 LBW cases (644) and 143 VLBW cases (132).
** IOM estimated 19% of 644 LBW cases (122) and 38% of 132 VLBW cases (50) require rehospitalization.
†† Based on 2% mortality of 776 cases (644 LBW plus 132 VLBW).
‡‡ 18.9% morbidity on 760 cases.

Table 5. Annual Cost Estimates for Treatment of Select Organic and Sensorineural Disorders

Disorder	Number of cases*	Cost/patient†	Total annual cost
Heart defects			$1,904,736
a) Teratology of Fallot (0.9%)	10	$ 3,663	$ 168,230
Less 0.5% "background"		$13,160	
Surgical Repair			
Hospital Costs (7.4 days)			
b) Ventricular Septal Defect (8.4%) only one-third need surgery	29	$ 3,663	$ 487,838
		$13,159	
Less 0.05% "background"			
Surgical Repair			
Hospital Cost (7.4 days)			
c) Atrial Septal Defect (4.9%)	58	$ 2,959	$ 934,844
Less 0.01% "background"		$13,159	
Surgical Repair			
Hospital Costs (7.4 days)			
d) Pulmonary Stenosis (2.7%)	32	$ 3,223	$ 313,824
Less 0.003% "background"		$ 6,584	
Surgical Repair			
Hospital Costs (5.7 days)			
Spina Bifida (1.8%)‡			
Less 0.04% "background"	21	$ 1,600	$ 216,489
Surgical Repair		$ 8,709	
Hospital Costs (12.5 days)			
Cleft Palate (8.9%)§			
Less 0.03% "background"	104	$ 2,500	$ 565,552
Surgical Repair		$ 2,938	
Hospital Costs (3.0 days)			
Serous Otitis Media w Myringotomy (93%)‖			
Less 12% "background"	953	$ 275	$1,252,242
Surgical Repair		$ 1,039	
Hospital Costs (1.3 days)			
Sensorineural Hearing Loss (29%)‖·¶			
Less 2% "background"	218	$ 480	$ 104,640
Inguinal Hernia (3.5%)			
Less 0.001% "background"	41	$ 968	$ 172,774
Surgical Repair		$ 3,246	
Hospital Costs (4.6 days)			
Hypospadias (5.8%)			
Less 0.001% "background"	68	$ 900	$ 296,480
Surgical Repair		$ 3,460	
Hospital Costs (4.3 days)			

* Incidence from Abel[5] extrapolated to annual 1,176 cases and corrected for "background" incidence.[69,72,73]

† Surgical fees at Detroit Medical Center and DRG approved rates.

‡ Includes renal ultrasound, voiding cystogram, consultation (urologist, neurologist, orthopedist, and geneticist), braces, chair, comprehensive visit to clinic.

§ Includes speech evaluation ($60) and therapy ($30/session, twice weekly).

‖ Based on Church and Gerkin[71] and extrapolated to annual FAS pop.

¶ Includes initial auditory screen ($75), hearing aid evaluation ($50), hearing aid orientation ($30), and hearing aid ($300).

in detecting anomalies.[5] Differences in the types of surveillance systems have been reviewed by Hexter et al.[7] Despite problems comparing data from different systems, they are useful in the present context for within group comparisons.

A surveillance study, reported by the Center for Disease Control (CDC)[29] based on hospital discharge diagnostic records of FAS collected from 1236 hospitals in the U.S. participating in its Birth Defects Monitoring Program, found that the incidence of FAS among blacks was about seven times higher than among whites and the rate among native Americans was over 30 times higher. Diagnosis was based on anomalies observed at, or within a few days after birth. However, the majority of the participating hospitals in this study reported fewer than 1000 births per year and therefore many large inner city hospitals were not included. Hutzel Hospital in Detroit, for example, delivers about 9000 babies to mainly black lower SES women each year, but was not a participant. Nor was Cleveland Metropolitan General Hospital, the site of a large prospective study on FAS.[24] Consequently, the number of minority children with FAS features seen at the sites participating in the CDC study is unlikely to be high. Physicians making the diagnosis may therefore be less experienced in differentiating affected children among minorities from nonaffected children, or may characterize minority features as "anomalous," relative to a prevailing white standard.

The surveillance study from California for 1983 to 1986[30] is derived from its Birth Defects Monitoring Program initiated in 1982 and includes registry data on 452,287 live births obtained from hospitals in 27 counties of the state. Any defects diagnosed during the first year are included. The system is unique in that information is obtained by specialists who routinely visit hospitals and genetics clinics where they personally review medical charts rather than relying on information coded by

Table 6. Alternate Methods of Estimating Costs for FAS Patients Requiring 24-Hr Residence Care due to Mental Retardation (MR)

Retrospective projection	Prospective projection
Based on incidence of FAS among mentally retarded	Based on MR among FAS patients
Total No. 24-hr MR residents = 205,336*	No. FAS cases/year = 1,176
No. FAS residents = 4,722†	53% FAS cases with MR/yr = 623‡
Median annual cost per each 24-hr resident = $22,885	*Less* 18% mortality rate up to age 21 = 511
	Total No. over 21 years = 10,731
	Less background MR prevalence of 2.3% = 10,484
Total annual cost for all FAS residents = $108,062,970	25% placement per ascertainment = 2,621§
Less personal consumption cost of $5,643 if individual were not institutionalized‖ = $26,646,246	*Less* 25% of total since none are placed in home prior to 5 years = 1,966
Net annual cost = $81,416,724	Median annual cost per each 24-hr resident = $22,885
	Total annual cost (1,966 × $22,855) = $44,991,910
	Less personal consumption cost = $11,094,138‖
	Net cost = $33,897,772
Average No. residents = 3,344	
Average total cost = $57,657,248	

* Based on Hill and Latkin.[79]
† Based on total of 205,336 residents and rate of 23/1,000.
‡ Based on incidence in clinical case literature.[5]
§ Based on Zigler and Cascione[80]; see also Grossman.[81]
‖ Department of Agriculture,[82] page 34.

Table 7. Summary of Annual Cost for Select Problems Related to FAS

		Percentage of total
Low birth weight	$12,390,940	16.62
Heart defects	$ 1,904,736	2.55
Spina bifida	$ 216,489	0.29
Cleft palate	$ 565,552	0.76
Serous otitis media	$ 1,252,242	1.68
Sensorineural auditory defects	$ 104,640	0.14
Inguinal hernia	$ 172,774	0.23
Hypospadia	$ 296,480	0.40
Mental retardation	$57,657,248	77.3
Total	$74,561,101	

nonspecialists. This study found an overall rate of FAS five times higher in blacks than whites.

The third surveillance study worth noting comes from the State of Washington for the years 1987 to 1988. A total of 142,800 live births were recorded during that period (La Mier, personal communication). Each reported FAS diagnosis in the registry was examined by a trained dysmorphologist to insure that the diagnosis complied with the criteria associated with FAS (La Mier, personal communication). Although Seattle was the site at which the first cases of FAS were noted, the number of FAS cases was very low with only five confirmed cases (one black, two native Americans, two whites). This is less than half the number of children identified by Jones and Smith in less than a year when they first discovered this syndrome.[3,8] Although the number of cases in the Washington registry is too low to make valid comparisons, it is interesting to consider that based on racial demographics, the incidence rates for blacks was seven times higher than for whites (0.14 vs. 0.02). Possibly there are now so few cases in this area because of the attention that has been focused on FAS in this part of the country. It is possible, of course, that ascertainment at birth may still be incomplete and rates are much higher than indicated by the Washington registry.

The surveillance study conducted in the province of British Columbia, Canada (Wong, unpublished study), was part of that province's longstanding Health Surveillance Registry. That data base was examined for the entire population and specifically for the native Indian population for the years 1973 to 1980. The rate of FAS among the native population was about 10 times higher than among the rest of the population (4.7 per 1000 vs. 0.4 per 1000). However, most of the native American cases came from Indians living on reserves. This could represent an actual increase in incidence among native Americans living on reserves compared to urban areas, especially if drinking rates are higher on reserves than elsewhere, or may reflect a bias in reporting. There are other biases as well. Many of the cases were not originally diagnosed as FAS but if the clinical information listed the mother as an alcoholic, that case was given greater scrutiny to see if the patient had disabilities that could be considered FAS, although formal criteria for FAS were not used (Wong, unpublished study). Other studies of FAS among native Canadian Indians have been criticized for similar biases.[50]

While there is a clear-cut consensus that FAS has a higher incidence among minorities in the U.S., the basis of this difference remains to be determined. If blacks and native American Indians are at risk for FAS due to some genetically linked susceptibility to alcohol's teratogenic effects,[51] it would be important to verify this finding so that additional prevention efforts could be marshaled and so that current limited resources could be more effectively targeted at them. On the other hand, it is possible that the higher rates of FAS associated with certain minority groups are due to characteristics of these populations which have nothing to do with FAS.

For example, two of the most common facial features associated with FAS are epicanthic folds and short palpebral fissures.[10] Native Americans have a genetic trait for epicanthic folds. The presence of such folds makes measurement of other facial features, e.g., palpebral fissure size, problematic. Blacks also have significantly different palpebral fissure sizes from whites.[52] Most studies of palpebral fissure size rely on Chouke's[53] norms which were based on whites. Thus, when race-related normative data are not used for diagnostic purposes, native American Indians and blacks will have a greater likelihood of being characterized as FAS because certain features that are normal for their own reference group are atypical for whites.

With respect to palpebral fissure size itself, actual measurements have been reported for only 15 out of the 188 cases described in the literature with this feature.[5] Short

palpebral fissure size thus appears to be more a subjective than objective facial anomaly in FAS and there is considerable disagreement among researchers as to its prevalence in this disorder. Hanson et al.[27] estimated the incidence of this anomaly at over 90% in FAS patients but this may have been based primarily on the black and Indian children examined by Jones and Smith[3,8] and Jones et al.[8] In Hanson et al.'s[27] prospective study reported somewhat later, only two FAS cases were noted and both were black. Majewski[54] found short palpebral fissures in only 11% of his FAS patients. When Majewski and Goeke[55] actually measured palpebral fissure sizes, they did not find it to be a specific effect related to FAS. Likewise, Debanne et al.[56] did not find shortened palpebral fissure size to be a specific effect of prenatal alcohol exposure in their prospective study of over 1000 infants.

These same arguments, viz., using race-related norms from one group to make judgments of another, and frequent nonobjective criteria being used as diagnostic features apply equally to other facial features used in the diagnosis of FAS, e.g., antimongoloid slant. It is very possible that examiner bias could contribute to the higher rate of FAS reported among native American Indians.[50]

Birth weight is also a problematic characteristic when comparing races. The percentage of low birth weight (LBW) infants (<2500 g) among whites in general is 5.7%. Among blacks in the U.S., the rate is 12.7%.[57] Black children are thus at risk for a diagnosis of FAS because of a trend for lower birth weight. One reason for lower birth weights among blacks is because a considerably greater proportion of black women 19 and under have children than whites[57] and low maternal age is a risk factor for LBW.

Since there are no growth charts for native Americans, researchers have relied on standard growth charts based primarily on whites.[58] If there is much disparity between the birth and growth weights of native Americans and whites, this would not be appropriate. Given the differences in birth weight between blacks and whites, there is probably a marked difference in birth weights and postnatal growth between native Americans and Caucasians. Since alcohol accounts for no more than 2% of the decrease in birth weight associated with prenatal alcohol exposure,[11,25,26,59,60] there is a possibility that the higher rates of FAS among blacks, and possibly among other minority groups, are due to experimenter bias or subject-related differences apart from alcohol use rather than either genetic susceptibility or associated environmental contributors to LBW and slowed growth.

Since both incidence estimates of FAS and the total number of children born in the various ethnic groups differ widely, we projected the numbers of black and white FAS cases in the U.S. on the basis of racial demographics (Table 3). This resulted in a much lower number of children born with FAS each year in the U.S. compared with our 1987 estimate: 1176 vs. 7024, respectively. Again, we emphasize that our previous estimate was based on combining prospective and retrospective studies. Since there are no prospective data for native Americans or other racial/ethnic groups, we did not include these numbers in our current calculations. Had we done so, the number of FAS cases would have undoubtedly been higher, but we are unable to estimate how much higher.

ESTIMATED COSTS

Our previous estimates of the economic impact of FAS were influenced by prior analyses by Russell,[61] Stanage et al.,[62] and Harwood and Napolitano.[63] Since the publication of these articles, only one additional study has appeared (Holzman, unpublished paper) besides our own.

We will not review the various abnormalities and medical problems associated with FAS here. These have been previously reviewed in depth.[5,65,66] Our estimates for the frequency of occurrence of many of these anomalies in conjunction with FAS are based on our last analysis, which includes an in depth analysis of 550 case studies.[5]

Growth

Pre- and postnatal growth retardation is one of the diagnostic features of FAS. Therefore, nearly every FAS patient is growth-retarded at birth, and the others may fall within the normal range at birth but are growth-retarded later. However, only a portion of these children require special treatment for small stature. To estimate costs due to FAS-related growth retardation, we again relied on the Institute of Medicine's[67] overall framework for estimating treatment costs for LBW infants. This framework includes several components: (1) initial hospitalization for intensive care; (2) cost of repeat hospitalization during the year for surviving children; and (3) noninstitutional, nonhospital morbidity costs for children surviving the first year of life.

At the time of our most recent survey (mid-1988), only 383 out of our known 550 case reports contained birth weight information.[5] The median birth weight for all those 383 cases, regardless of gestation length, was 2100 g compared with 3370 g for all infants born in the United States.[68] Birth weight for term FAS infants, 38 weeks or more, was 2290 g.

The percentage of FAS children with low birth weight (LBW) (<2500 g) was 77%. Extrapolating to the total FAS population results in an estimated 906 cases (77% of 1176). If the percentage of LBW infants born each year in the U.S. (6.8%), regardless of cause, is subtracted from the number of LBW infants due to FAS, the resulting number of cases with LBW each year as a result of FAS is 844. This assumes that all such cases would have occurred anyway whereas it is reasonable that some were due to alcohol exposure. Since it is not possible to determine the proportion of these incremental cases, we have taken the more conservative approach and subtracted them all. The

same rationale has been used to estimate costs associated with other FAS-related anomalies.

The percentage of the 844 cases with FAS-related moderate LBW (1500–2500 g) is 83% (701) and 40% of these will need intensive care (280 cases). The remaining 17% of the 844 cases (143) are very LBW (<1500 g), and all will require intensive care (see Table 4).

Our estimates for rehospitalization costs during the 1st year were again based on the Institute of Medicine's mortality rate of eight per 100 since relevant statistics for FAS children are still not available. This reduced the number of cases potentially requiring rehospitalization to 776 (92% of 844) comprising about 644 (83%) low and 132 (17%) very LBW children. Since children with low and very LBW each have different probabilities of rehospitalization and will require different durations of rehospitalization (12.5 and 16.2 days, respectively), costs for each group were estimated separately (see Table 5) using the IOM's probability estimates of 19% and 38% rates of rehospitalization for LBW (122) and VLBW (50) cases, respectively.

To estimate long-term single-year morbidity costs, we again used the IOM's estimate of an additional 2% mortality and 18.9% morbidity for LBW infants surviving the 1st year. Among the 776 (92% of all live births) who survive their neonatal period, 760 (98%) are expected to survive their first year and 144 are expected to have additional costs due to morbidity (760 × 0.189). Based on the total number of cases and estimated percentages of children requiring care for LBW, and subtracting the number of cases that would be LBW without FAS, we estimated an annual incremental cost of FAS-related growth retardation at about $12.4 million (see Table 4). This estimate is about $50 million lower than our previous estimate which was based on a higher incidence of FAS and did not allow for "background" cases of LBW.

Organic Anomalies

Numerous organic anomalies are associated with FAS, but the frequency for all anomalies is as yet not fully defined and many do not require corrective surgery. The frequency and costs associated with those typically requiring surgical correction, e.g., cleft palate, neural tube defect, heart defects are documented in Abel[5] and are as follows:

Cleft palate was reported for 8.9% of the 550 cases in the literature.[5] Since cleft palate is easily identified and requires immediate attention, the prevalence is likely reliable. The same rationale holds for the 1.8% cases of spina bifida.[5] "Background" prevalences for these two anomalies are 0.03% and 0.04%, respectively.[69]

Ventricular and atrial septal defects occurred in about 8.5% of FAS cases.[5] The severity of these anomalies varies, however, and only about one-third of these cases require surgery.[70] Tetralogy of Fallot was reported in 0.9% of the cases and pulmonary stenosis in 2.7%.[5] Each of these requires surgery. "Background" rates for these anomalies are less than 0.1%.[69] Patent ductus arteriosus was reported in 11 cases,[5] but the persistence of this anomaly was not indicated, so that we could not determine how many cases required surgery. Sensorineural auditory anomalies with recurrent serous otitis media requiring myringotomy is a common occurrence in FAS[71] and accounts for a considerable amount of the medical costs for FAS. Other anomalies and "background rates" are listed in Table 5.

Hospital charges for each anomaly were based on Diagnostic Related Group (DRG) charges used at Hutzel Hospital in Detroit.

Mental Retardation

In our previous report, we reviewed several of the problems related to estimating the costs associated with mental retardation. The main problem from a prospective view relates to how the condition is defined. Definition is more easily dealt with in retrospective studies, since the criterion for mental retardation is placement in an appropriate facility.

Our revised method for estimating institutionalization costs due to mental retardation was initially similar to that we previously reported. Costs were estimated in two ways—first, by determining the proportion of mentally retarded people already in special facilities for whom FAS has been diagnosed and extrapolating to the total mental retardation population. This estimate was then "corrected" for personal item costs that would be incurred whether the individual were mentally retarded or not (e.g., food, clothing).

The estimated prevalence of FAS in institutionalized persons in our previous study was based on four studies.[74–77] The present report is based on these studies and additional data from Tanaka et al.[78] This resulted in an overall prevalence of mental retardation in institutes due to FAS at 23 cases per 1000, which is slightly below our previous estimate of 24.2 per 1000. When "corrected" for personal item costs that would be incurred regardless of institutionalization, the estimated costs of care for these people were about $81 million (see Table 6).

People with borderline mental retardation (IQ scores between 70–85) are capable of semi-independent living and can function in community settings with ambulatory care and special education, but are not included in our cost estimates because there are no estimates from retrospective studies of the number of such people with FAS. However, we were able to make this assessment for our prospective analysis.

In our second procedure, we adopted a prospective approach and determined the prevalence of mental retardation among those with FAS, for a cohort up to age 21 (the age of the oldest patient in the facilities thus far examined, see below). As in our previous effort, we did not include estimates for decreased worker productivity or related economic impact owing to the difficulties in

making such an estimate.[83] However, in this analysis, we subtracted costs for personal items and we took into account the age at which individuals are placed in institutions.

Based on the clinical literature,[5] 53% of all FAS patients have an IQ below 70 (average I.Q. for FAS cases is about 67). The total number of FAS patients eligible for placement in a residential facility each year is, therefore, 623 (53% of an annual 1176 patients born with FAS).

Since children born to alcoholic women have a high neonatal and infant mortality rate,[6] we relied on the same 18% mortality rate for these children used in our previous report. This resulted in an estimated 511 of the 623 eligible FAS individuals being admitted for care to residential facilities each year.

The oldest patient identified in the retrospective studies was 21 years of age. To compare the prospective and retrospective projections, the number of individuals with mental retardation due to FAS who would be born over a 21-year period was estimated and then corrected for an ascertainment rate of 25%,[79,84] and a further 25% decrease due to admission beginning only after 5 years of age since children are generally not institutionalized at an age younger than five.[85] Based on these considerations, and correcting for a background prevalence of 2.3%[80] and personal consumption costs that would have been incurred in any case,[82] the prospectively estimated annual total cost for full-time residential patients is about $33.8 million (see Table 6). Averaging the retrospective and prospective estimates yields an annual average cost of about $57.7 million due to FAS.

Using a similar rationale, we estimated costs associated with semi-independent FAS cases requiring supervised support. The median cost of providing such care is $6,223 per person per year.[84] About 33% of all cases of FAS in the literature have IQs in the range of 70–85[5] so that the number of potential individuals with FAS in this category is 388 per year. Correction for postnatal mortality results in 350 cases (388 × 0.92 × 0.98). However, most of these cases would not require such support until they were 21 years of age, after which the annual costs would be $2,178,050 ($6,223 × 350). Since we do not know the life span of these individuals, we cannot be certain how many years beyond 21 to project costs and, therefore, we have only estimated what costs might be on a minimal basis rather than including them in our overall estimate.

Summary

Our estimated total annual cost for FAS is $74.6 million (Table 7). Of this, about 78% is accounted for by costs associated with mental retardation and LBW. This estimate is considerably less than our previous estimate of $321 million owing to the considerable reduction in estimated cases of FAS. As in our previous study, pain and suffering and other aspects contributing to the value of human life were not taken into account. Although attempts have been made to place these in terms of dollars, they are at best problematic.[83] We also did not include estimates for anesthesia associated with surgical procedures because these are billed on an hourly basis and vary considerably within procedures.

These economic estimates were based only on FAS and represent only one aspect of the broad spectrum of abnormalities associated with prenatal alcohol exposure. As previously mentioned, we focused on FAS because criteria have been established for its diagnosis. Our estimates did not take into account costs associated with treating reproductive damage due to alcohol nor related consequences, such as increased rates of spontaneous abortion. This would also add to the medical costs associated with prenatal alcohol exposure, but we do not have enough data to determine a frequency estimate above baseline. We also do not have enough data to estimate potential costs stemming from cerebral palsy or meningitis, which may also be increased[18] (Holzman, unpublished paper), or from other problems such as attention deficit disorder and speech pathology. Nor did we include estimates for semi-independent living for individuals with borderline mental retardation. We have instead restricted estimates to the strictly defined features of FAS.[2] These estimates are, we believe, conservative lower limits.

Estimates such as ours are completely dependent on the definitions and criteria used for FAS. It is, of course, likely that the same criteria have not been used by each clinician in making a diagnosis of FAS. This may have resulted in over-diagnosis in some circumstances, especially for minority children. The obverse possibility is that many cases of FAS go undetected because recognition of FAS requires some sophistication. A revised list of features based on an analysis of the reported frequency of occurrence of several medical disorders has been proposed.[5] Adoption of these new criteria would reduce the number of "false positives and negatives."

Regardless of fine points in methodology, our conservative annual cost for FAS in the United States of about $74.6 million constitutes a high cost by any reasonable standard and represents a benchmark against which costs of potential prevention strategies may be judged.

ACKNOWLEDGMENTS

This study was supported by grant P50 AA07606. We thank Drs. J. Hannigan and M. Church for critical comments.

REFERENCES

1. Rosett HL: A clinical perspective of the fetal alcohol syndrome (editorial). Alcohol Clin Exp Res 4:119–122, 1980

2. Sokol RJ, Clarren SK: Guidelines for use of terminology describing the impact of prenatal alcohol on the offspring. Alcohol Clin Exp Res 13:597–598, 1989

3. Jones KL, Smith DW: Recognition of the fetal alcohol syndrome in early infancy. Lancet 2:999–1001, 1973

4. Abel EL, Welte JW: Publication trends in fetal alcohol, tobacco and narcotic effects. Drug Alcohol Depend 18:107–114, 1986

5. Abel EL: Fetal Alcohol Syndrome. Oradell NJ, Medical Economics, 1990

6. Abel EL, Sokol RJ: Incidence of fetal alcohol syndrome and economic impact of FAS-related anomalies: Drug alcohol syndrome and economic impact of FAS-related anomalies. Drug Alcohol Depend 19:51-70, 1987

7. Hexter AC, Harris JA, Roeper P, Croen LA, Kruger P, Grant D: Evaluation of the hospital discharge index and the birth certificate as sources of information on birth defects. Public Health Rep 105:296-306, 1990

8. Jones KL, Smith DW, Ulleland CN, Streissguth AP: Pattern of malformation in offspring of chronic alcoholic mothers. Lancet 1:1267-1271, 1973

9. Pierog S, Chandavasu O, Wexler I: The fetal alcohol syndrome: Some maternal characteristics. Int J Gynaecol Obstet 16:412-415, 1979

10. Clarren SK, Sampson PD, Larsen J, Donnell DJ, Barr HM, Bookstein FL, Martin DC, Streissguth AP: Facial effects of fetal alcohol exposure: Assessment by photographs and morphometric analysis. Am J Med Genet 26:651-666, 1987

11. Hingson R, Alpert JJ, Day N, Dooling E, Kayne H, Morelock S, Oppenheimer E, Zuckerman B: Effects of maternal drinking and marijuana use on fetal growth and development. Pediatrics 70:539-546, 1982

12. Qazi QH, Mariano E, Milman DH, Beller E, Crombleholme A: Abnormalities in offspring associated with prenatal marihuana exposure. Dev Pharmacol Ther 8:141-148, 1985

13. Zuckerman B, Frank DA, Hingson R, Amaro H, Levenson SM, Kayne SM, Parker S, Vinci R, Aboagye K, Fried LE, Timperi R, Bauchner H: Effects of maternal marijuana and cocaine use in fetal growth. N Engl J Med 320:762-768, 1989

14. Sokol RJ, Ager J, Martier S, Debanne S, Ernhart C, Kuzma J, Miller SI: Significant determinants of susceptibility to alcohol teratogenicity. Ann NY Acad Sci 477:87-102, 1986

15. Bell R, Lumley I: Alcohol consumption, cigarette smoking and fetal outcome. Community Health Stud 13:484-491, 1989

16. Gibson GT, Baghurst PA, Colley DP: Maternal alcohol, tobacco, and cannabis consumption and the outcome of pregnancy. Aust N Z J Obstet Gynaecol 23:15-19, 1983

17. Lumley J, Correy JF, Newman NM, Curran JT: Cigarette smoking, alcohol consumption and fetal outcome in Tasmania. Aust N Z J Obstet Gynaecol 23:33-40, 1985

18. Olegard R, Sabel KG, Aronsson M, Sandin B, Johnsson PR, Carlsson C, Kyllerman M, Iversen K, Hrbek A: Effects on the child of alcohol abuse during pregnancy: Retrospective and prospective studies. Acta Paediatr Scand [Suppl] 275:112-121, 1979

19. Larsson G: Prevention of fetal alcohol effects: An antenatal program for early detection of pregnancies at risk. Acta Obstet Gynecol Scand 62:171-178, 1983

20. Wright JT, Barrison IG, Lewis IG, MacRae KD, Waterson EJ, Toplis PJ, Gordon MG, Morris NF, Murray-Lyon IM: Alcohol consumption, pregnancy, and low birth weight. Lancet 3:663-665, 1983

21. Plant ML, Plant MA: Maternal use of alcohol and other drugs during pregnancy and birth abnormalities: Further results from a prospective study. Alcohol Alcohol 23:229-233, 1988

22. Waterson EJ, Murray-Lyon IM: Drinking and smoking patterns amongst women attending an antenatal clinical. II. During pregnancy. Alcohol Alcohol 24:163-173, 1989

23. Quellette EM, Rosett HL, Rosman NP, Weiner L: Adverse effects on offspring of maternal alcohol abuse during pregnancy. N Engl J Med 297:528-530, 1977

24. Sokol RJ, Miller SI, Reed G: Alcohol abuse during pregnancy: An epidemiologic study. Alcohol Clin Exp Res 4:135-145, 1980

25. Tennes K, Blackard C: Maternal alcohol consumption, birth weight, and minor physical anomalies. Am J Obstet Gynecol 138:774-780, 1980

26. Kuzma JW, Sokol RJ: Maternal drinking behavior and decreased intrauterine growth. Alcohol Clin Exp Res 6:396-402, 1982

27. Hanson JW, Streissguth AP, Smith DW: The effects of moderate alcohol consumption during pregnancy on fetal growth and morphogenesis. J Pediatr 92:457-460, 1978

28. Little RE: Moderate alcohol use during pregnancy and decreased infant birth weight. Am J Public Health 67:1154-1156, 1977

29. Chavez GF, Corder JF, Becerra JE: Leading major congenital malformations among minority groups in the United States. MMWR 37:17-24, 1988

30. Croen L, Schulman J, Roeper P: Birth Defects in California. California Birth Defects Monitoring Program. Sacramento, California, 1990

31. Deleted in proof.

32. Barrison IG, Waterson EJ, Murray-Lyon I: Adverse effects of alcohol in pregnancy. Br J Addict 80:11-22, 1985

33. Fox SH, Brown C, Koontz AM, Kessel SS: Perceptions of risks of smoking and heavy drinking during pregnancy: 1985 NHIS findings. Public Health Rep 102:73-79, 1987

34. Alpert JJ, Day N, Dooling E, Hingson R, Oppenheimer E, Rosett HL, Weiner L, Zuckerman B: Maternal alcohol consumption and newborn assessment: Methodology of the Boston City Hospital Prospective Study. Neurobehav Toxicol Teratol 3:195-201, 1981

35. Marbury MC, Linn S, Monson RP, Schoenbaum S, Stubblefield PG, Ryan KJ: The association of alcohol consumption with outcome of pregnancy. Am J Public Health 73:1165-1168, 1983

36. Weiner L, Rosett HL, Edelin KC, Alpert JJ, Zuckerman B: Alcohol consumption by pregnant women. Obstet Gynecol 61:6-12, 1983

37. Russell M, Bigler LR: Screening for alcohol-related problems in an outpatient obstetric-gynecologic clinic. Am J Obstet Gynecol 34:4-12, 1979

38. Kruse J, Lefevre M, Zweig S: Changes in smoking and alcohol consumption during pregnancy: A population based study in a rural area. Obstet Gynecol 67:627-632, 1986

39. Kuzma JW, Kissinger DG: Patterns of alcohol and cigarette use in pregnancy. Neurobehav Toxicol Teratol 3:211-221, 1981

40. Mills J, Graubard B: Is moderate drinking during pregnancy associated with an increasing risk for malformation? Pediatrics 80:309-314, 1987

41. Harlap S, Shiono PH: Alcohol, smoking, and incidence of spontaneous abortions in the first and second trimester. Lancet 2:173-176, 1987

42. Stephens CJ: Alcohol consumption during pregnancy among southern city women. Drug Alcohol Depend 16:19-29, 1985

43. Kline J, Shrout P, Stein Z, Susser M, Warburton D: Drinking during pregnancy and spontaneous abortion. Lancet 2:176-180, 1980

44. Brooten D, Peters MA, Glatts M, Gaffney SE, Knapp M, Cohen S, Jordan C: A survey of nutrition, caffeine, cigarette and alcohol intake in early pregnancy in an urban clinic population. J Nurse Midwifery 32:85-90, 1987

45. Streissguth AP, Barr HM, Martin DC: Maternal alcohol use and neonatal habituation assessed with the Brazelton Scale. Child Dev 54:1109-1118, 1983

46. Little RE, Schultz FA, Mandell W: Drinking during pregnancy. J Stud Alcohol 37:375-379, 1976

47. Streissguth AP, Martin DC, Buffington VE: Identifying heavy drinkers: A comparison of eight alcohol scores obtained on the sample, in Sexias FA (ed): Currents in Alcoholism. New York, Grune and Stratton, 1977, pp 395-420

48. Bingol N, Schuster C, Fuchs M, Iosub S, Turner G, Stone RK, Gromisch DS: The influence of socioeconomic factors on the occurrence of fetal alcohol syndrome. Adv Alcohol Subst Abuse 6:105-118, 1987

49. May PA, Hymbaugh KJ, Aase JM, Samet JM: Epidemiology of fetal alcohol syndrome among American Indians of the Southwest. Soc Biol 30:374-387, 1983

50. Bray DH, Anderson PD: Appraisal of the epidemiology of fetal alcohol syndrome among Canadian native peoples. Can J Public Health 80:42-45, 1989

51. Sokol RJ, Smith M, Ernhart CB, Baumann R, Martier SS, Ager

JW, Morrow-Tlucak M: A genetic basis for alcohol-related birth defects (ARBD)? Alcohol Clin Exp Res 13:343, 1989 (abstr)

52. Fuchs M, Iosub S, Bingol N, Gromisch DS: Palpebral fissure size revisited. J Pediatr 96:77–78, 1980

53. Chouke KS: The epicanthus or mongolian fold in Caucasian children. Am J Phys Anthropol 13:255, 1929

54. Majewski F: Alcohol embryopathy: Some facts and speculations about pathogenesis. Neurobehav Toxicol Teratol 3:129–144, 1981

55. Majewski F, Goeke T: Alcohol embryopathy: Studies in Germany, in Abel EL (ed): Fetal Alcohol Syndrome, vol 2, Human Studies. Boca Raton, CRC Press, 1982, pp 65–88

56. Debanne S, Sokol RJ, Martier S, Golden N, Miller SJ: Are short palpebral fissures really an alcohol-related birth defect? Alcohol Clin Exp Res 8:87, 1984

57. Feinleib M: Advance report of final mortality statistics, 1987. Monthly Vital Statistics Report 38(3) (Suppl), 1989

58. Streissguth AP, Ladue RA, Reynolds SP: A manual on adolescents and adults with fetal alcohol syndrome with reference to American Indians. Seattle, University of Washington, 1988

59. Plant ML: Women, Drinking and Pregnancy, ed 2. London, Tavistock, 1985

60. Rosett HL, Weiner L, Edelin KC: Treatment experience with pregnant problem drinkers. JAMA 249:2029–2033, 1983

61. Russell M: The impact of alcohol-related birth defects (ARBD) on New York State. Neurobehav Toxicol 2:277–283, 1980

62. Stanage WF, Gregg JB, Massa LJ: Fetal alcohol syndrome: Intrauterine child abuse. SD J Med 36:35, 1983

63. Harwood HJ, Napolitano DM: Economic implications of the fetal alcohol syndrome. Alcohol Health Res World 10:38–43, 1985

64. Deleted in proof

65. Abel EL: Fetal Alcohol Syndrome/Fetal Alcohol Effects. New York, Plenum Press, 1984

66. Rosett HL, Weiner L: Alcohol and the Fetus. New York, Oxford University Press, 1984

67. Institute of Medicine: Preventing Low Birthweight. Washington DC, National Academy Press, 1985

68. Wegman ME: Annual summary of vital statistics—1986. Pediatrics 80:817–827, 1987

69. Taffel S: Congenital anomalies and birth injuries among live births: United States, 1973–74. US Department of Health, Education, and Welfare, Public Health Service, Hyattsville, Maryland, 1978

70. Dupuis C, Dehaene P, Deroubaix-Tella P, Blanc-Garin AP, Rey C, Carpentier-Courault C: 'Les cardiopathies des enfants nés de mère alcoolique.' ['Cardiac diseases in children born to alcoholic mothers.'] Arch Mal Coeur Vaiss 71:565–572, 1978

71. Church MW, Gerkin KP: Hearing disorders in children with fetal alcohol syndrome: Findings for case reports. Pediatrics 82:147–154, 1988

72. Howie VM, Ploussard JH, Sloyer J: The "otitis-prone" condition. Am J Dis Child 129:676–678, 1975

73. Kileny P, Robertson CMT: Neurological aspects of infant hearing assessment. J Otolaryngol 14:34–39, 1984

74. Fryns JP, Deroover J, Parloir C, Gaffaux P, Lehas E, Van den Berg H: The fetal alcohol syndrome. Acta Paediatr Belg 30:117–121, 1977

75. Mena MR, Casanueva VE, Fern'andez ER, Carrasco R, Perez H: Fetal alcohol syndrome at schools for mentally handicapped children in Concepcio'n, Chili. PAHO Bull 20:157–169, 1986

76. Hagberg B, Kyllerman M: Epidemiology of mental retardation: A Swedish survey. Brain Dev 5:441–449, 1983

77. Shanske AL, Kazi R: Prevalence of the fetal alcohol syndrome in a developmental clinic population. Am J Hum Genet 32:128A, 1980 (abstr)

78. Tanaka H, Arima M, Ishizuka H, Suzuki N, Takashima H: Fetal alcohol syndrome in Japan. Jpn J Med 2897:27–30, 1976

79. Hill BK, Latkin KC: Classification of residential facilities for mentally retarded people. Minneapolis: Center for Residential and Community Services, University of Minnesota, Department of Educational Psychology, 1984

80. Zigler E, Cascione R: Neonatal retardation: An overview, in Gollin ES (ed), Malformations of Development, New York, Academic Press, 1984, pp 69–94

81. Grossman HJ: Classification In Mental Retardation. Washington DC, American Association in Mental Deficiency, 1983

82. Department of Agriculture: Family Economics Review, Number 2. Washington DC, Department of Agriculture, 1984

83. Eisenberg L: Prevention: Rhetoric and reality. J R Soc Med 77:268–280, 1984

84. Hill DE, Slikker Jr, W, Goad PT, Bailey JR, Szisak TJ, Hendrick AG: Maternal, fetal, and neonatal elimination of ethanol in nonhuman primates. Dev Pharmacol Ther 6:259–268, 1983

85. Barden HS, Kessel R, Schuett VE: The costs and benefits of screening for PKU in Wisconsin. Soc Biol 31:1–17, 1984